

How Not to Run Research Councils (Indian style)

THE sad case of Dr V. H. Shah's suicide in New Delhi last week is a telling symptom of the malaise which afflicts publicly supported research in India (see page 130). Whether Dr Shah is right or wrong in suggesting that he should have been preferred to the one of the two men recently appointed to the two senior posts in agronomy at the Indian Agricultural Research Institute and the Indian Council for Agricultural Research is beside the point. The truth is that these organizations, like many other of the research organizations supported by the Government of India, are too rigid, too hierarchical and too directly exposed to political pressure and personal log-rolling. In one respect, at least, Dr Shah's suicide has been counter-productive in that it has exposed the agricultural research organizations more directly to political pressure from outside, which is why the Minister of Agriculture, Mr Fakhruddin Ali Ahmed, is to be congratulated for having denied a parliamentary inquiry. It is to be hoped that his resolution will survive the next few weeks. But although there is some hope that the internal review of the Indian Council for Agricultural Research now under way may be able to remedy some of the causes of those among Dr Shah's complaints which are legitimate, the chance is very small that the outcome will be a sufficiently radical transformation of the present state of affairs.

Nobody will dispute that younger scientists in Indian laboratories are frequently kept under the thumbs of their more senior colleagues, but it is unrealistic to single out one research organization for blame or even to suppose that the hierarchy can become less cramping until scientists themselves set much less store than they do at present on the acquisition of formal qualifications for promotion—not merely university degrees and diplomas but also the tally of published articles in the literature. (Absurdly, in some circles at least, one article in *Nature* is as good for a man's advancement as half-a-dozen in the Indian scientific press.) The need is somehow to create within the organizations such as the Indian Council for Scientific and Industrial Research and the Indian Council for Agricultural Research a system of organizations which is flexible enough to allow people at all levels to contribute towards what should be a common objective. If this should entail that relatively junior scientists should frequently be seen to be more expert, or more knowledgeable, than their betters, that is merely a sign of what creative research is like.

Outside India but also at places such as the Bhabha Atomic Research Centre and at internationally reputed centres such as the Tata Institute for Fundamental Research, laboratories are increasingly populated by bright young men and women who are expected and are alarmingly able to hold their own intellectually with the grey-beards. In circumstances like these, the authority of senior people derives as much from their capacity to listen well as from their own current competence in research.

Leadership is as important as innovation, and a laboratory's success depends largely on the skill with which its head can act as an impresario for his younger colleagues. Although in the past few years there have been welcome signs that this principle is gaining ground, at the present rate a long time will pass before scientists at all levels in government research will be as free as they would like.

Change could be quicker if the Government of India were less directly concerned with the administration of the research councils. As things are, the councils responsible for scientific and industrial research, agricultural research and medical research are presided over by the Cabinet Minister from whose budget funds are provided, and this personage—with interests and ambitions usually quite outside research—is formally responsible for all appointments. The result is that there are perennial arguments about the propriety of appointments, while the rates at which scientific workers are paid are closely linked with the antiquated pay scales of the Indian Civil Service as a whole. Inevitably, quite minor grievances become publicly political issues, and are not dealt with where they should be dealt with—internally. Worse still, the disparity between the earnings of junior and senior people is too great for health and comfort. By comparison, the laboratories of the Atomic Energy Commission are lucky that the Chairman of the Atomic Energy Commission is almost by definition a scientist with roots in research, that the Department of Atomic Energy is constitutionally responsible directly to the Prime Minister and that they are in any case a long way from Delhi. On all the evidence, the most urgent need is that the ministers responsible for research should practise what they preach, and grant the research councils a measure of meaningful autonomy.

The way in which one of the immediate consequences of Dr Shah's suicide has been the mounting of a personal attack on Dr M. S. Swaminathan, the Director-General of the Indian Agricultural Research Council, is at once a sign of how urgent is the need for change and a potential danger to the reputation of Indian science overseas. For Dr Swaminathan is a scientist of the highest reputation, personally responsible for much of the remarkable progress which has been made in Indian agriculture in the past few years. If the inspiration of the Green Revolution has been the development of new strains of wheat and rice in Mexico and the Philippines, its practical application in India has been to a large extent Dr Swaminathan's doing. If now, three months after taking over his new job, he should be pilloried for the long-standing deficiencies of the organization he has inherited and if—as seems to be the case—some of his critics are in effect complaining at his political friends, it is hard to see how the Government of India will in future be able to recruit good men to organize public research. Worse still, it is hard to see how Indian science will earn the credit overseas to which it is entitled.



The Pentagon and Basic Science

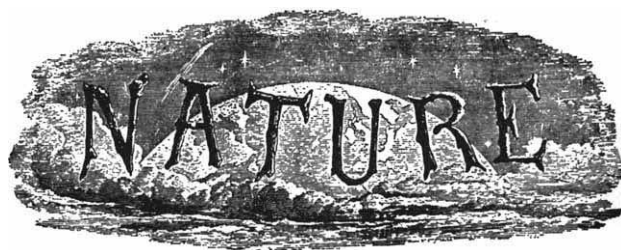
SEVERAL years have gone since the Department of Defense in the United States was widely and fairly regarded as a source of funds for basic research. Although the scale of expenditure under this heading is still quite large, by standards applicable elsewhere, and will amount to 15 per cent or thereabouts of what the Federal Government does to help basic science, the time is long since past when the armed services were able to support long-term research projects not merely because these were of potential scientific importance but because support of such a kind could be reckoned in the long run to contribute to the strength of American universities, to the supply of skilled people in science and engineering and ultimately to the strategic force of American policies, not merely in military fields but in economic fields as well. No doubt the transformation which there has been is a great comfort to academics embattled with students who are increasingly prepared to boycott lectures if it seems that there is a whiff of involvement with national security, and there are more lasting arguments than that for a permanent shift of the source of support for science to those agencies of government whose job it is to support basic research as such. Yet the transformation which has come about in the past few years is not merely of practical importance in the increasingly taut scramble for funds by American universities and colleges but also raises important questions for societies elsewhere.

Historically, the involvement of the Department of Defense in American science dates from the zeal with which the Office of Naval Research, more than a quarter of a century ago, set out on its unprecedented programme of support for basic science. In retrospect, some of the reasons given for these activities are enough to set a man back on his heels. The zoology of dolphins was, for example, held to be of potential relevance to military affairs by the paper-thin argument that nobody could be sure that isolated dolphin brains would not, in due course, turn out to be more convenient devices for flying military aircraft than ordinary bulky human beings. At this period, it was possible for the Office of Naval Research, followed by other departments of the military services, to rely on the ignorance in Congress and among their military bosses of the relationship between discovery and application—tenuous as it is—to ensure that the shallowest excuses for supporting basic science would be sufficient. To be sure, these generous agencies were able to justify their open-handedness to themselves by the argument that the money was being spent in the national interest, in the cause of helping university departments and other institutions to be strong. By the time that Mr Robert McNamara launched his Project Themis in the mid-1960s, with the objective of giving strictly institutional support and not support for particular research projects to university departments with promise of one kind or another, times had changed. The National Science Foundation was stronger, and there was more reason to suspect that the scale of intellectual effort in basic science was enough to sustain itself. By 1970, the climate had changed so much that Senator Mansfield was able to add to the Military Services legislation a requirement that the Pentagon should spend money on basic research only when this

could be seen to be directly relevant to military development. Although this has been amended military expenditure on basic science is now a less important part of the whole in the United States than it has ever been.

What are the consequences? The most awkward change has been a diminution of the scale of support for basic science in the United States. The budget of the National Science Foundation has grown in the past few years, but not enough to compensate for the extent to which the Department of Defense and the other agencies of the United States government have been compelled to trim their sails. To make things worse, the foundation has, off its own bat, set out to invest more of its funds in programmes related to technological development than it has yet been able to demonstrate that it can usefully spend. In the long run, the effects of the present strained circumstances of American universities will leave a permanent mark on the development of American science, even though it may in the more immediate future be something of an advantage that "fat" as it is called will be excised from the system. It is less important that the new balance of expenditure will reduce the extent to which applicants for grants for scientific research can hope to play off one agency against another. It has never been a welcome feature of the American system that less good grant applications could bounce from one committee to another until, sometimes by chance, they found a welcome.

100 Years Ago



Newspaper Science

THE general public cannot fail to acquire some very extraordinary as well as erroneous notions about many subjects relating to the progress and application of the different branches of Natural Science, if we are to judge from sundry scraps of information, daily communicated or reproduced for their instruction, in the columns of even the most influential newspapers. Amongst recent examples of this style of information we might refer to the following:—

Geography.—Under the heading, "Oysters from South America," we find in the *Times* of May 16, the announcement that the steamer *Kaffraria* had last Sunday "arrived at Hull from Norfolk, Virginia, having on board a cargo consisting of 500 or 600 tons of oysters, &c."

Metallurgy.—The *Engineer* of April 12, in a paragraph on early iron making at Merthyr Tydvil, in South Wales, must rather astonish metallurgists by writing of "bones supplying sulphate of lime" in the process.

Architecture.—In a somewhat elaborate article on the new so-called Selenitic mortar, which in reality takes its name from the introduction of a little sulphate of lime, which when native forms the mineral called selenite in its manufacture, we are informed that "the name given to the improved mortar indicates to a certain extent the nature of the improvement; that it is in the direction of combining *selenious* acid with a base," &c. It would, indeed, be good tidings to chemists to find that selenious acid had become so cheap as to allow of its being used for such purposes; unfortunately, however, the last price lists inform us that selenium, from which it is made, still costs three shillings per drachm.

From *Nature*, 6, 60, May 23, 1872.

OLD WORLD

Close of Play for the Select Committee

MR JOHN DAVIES, Secretary of State for Trade and Industry, last week failed to raise the hopes of the Select Committee on Science and Technology that the government would appoint a Minister for Research and Development. Appearing before the committee at the last public meeting of its enquiry into the state of government research and development, Mr Davies said that he could not see the advantages of having such a minister. The select committee recommended in a recent report that such a minister be appointed (see *Nature*, 237, 63; 1972).

Mr Davies's distinctly cool attitude towards the proposal arises because most research and development carried out by government departments is tied up with specific projects, and is not a case of research for the sake of research. This kind of research would remain in the care of the departments even if a minister were appointed, said Mr Davies, and in these circumstances a Minister for Research and Development would face difficulties because "vast areas of research and development would not be in his control".

Mr Davies was similarly sceptical of the select committee's recommendation that government research and development should be formulated on a five year rolling basis. If such a plan were instituted, said Mr Davies, it must have a "substantial contingency element" because "so much of the DTI's research and development programme arises from meetings and projects". But Mr Davies did point out that some 10 per cent of the DTI's research and development could be formulated on a five year basis and therefore could be put under the aegis of a Minister for Research and Development.

Mr Davies said that there would be "substantial changes" in collaborative ventures with Europe once Britain joins the European Communities. He considers that the industries which would benefit most would be those involved in nuclear systems and aerospace; computer technology would reap the advantages eventually but on a longer time scale.

No predictions were made by the secretary of state about Britain's future policy towards ELDO. In fact no decision on Britain's future aerospace commitments will be made, according to Mr Davies, until the present British study of the post-Apollo programme is completed in the autumn of this year.

In spite of Mr Davies's enthusiasm for collaborative research and develop-

ment programmes within Europe, a note of reserve was evident when he said that it is not easy to get such European cooperative programmes off the ground. Mr Davies did, however, say that he thought changes would occur much more rapidly once Britain is in the EEC.

Earlier last week Mr Michael Heseltine, Minister for Aerospace, also gave evidence to the select committee. Under considerable pressure from the members of the committee he outlined the possible areas of research and development to be covered by the requirements boards which the Department of Trade and Industry plans to introduce this autumn. He emphasized that these are only his first thoughts and that they may well change.

The boards, coming in the wake of Lord Rothschild's customer-contractor principle, are intended to act as customers within DTI spending about £25

million of the £200 million that is the DTI's civil research budget. The boards will buy the research the department feels it needs from either its own research establishments, the non-nuclear arm of the Atomic Energy Authority, industry or the universities. In time the boards will also handle the knotty problem of the industrial research associations.

Mr Heseltine said that he envisages between six and ten boards covering the areas of standards and metrology, marine and maritime technology, mechanical engineering and machine tools, materials, chemical and mineral processes and plant, computers and electronics; there may also be a board to deal with miscellaneous matters. Mr Heseltine also said that he is contemplating boards for waste and effluent technology, safety and health, and for the laboratory of the government chemist.

GRADUATE EMPLOYMENT

Plugging them in

A COMPUTER placement service to help graduates find jobs is to come into operation in a trial form this October. The service, known as CAP (Computer Assisted Placement), will be available at sixteen universities and colleges this autumn and more than 100 employers plan to take part.

The scheme is to be run by a non-profit making company set up by the Standing Conference of Employers of Graduates (SCOEG) whose 200 member companies include many of the large graduate employers—Shell and Metal Box for example. The service will be free to students, finance coming from the participating companies.

The scheme, which was discussed in detail by the Standing Conference of University Appointments Services (SCUAS) last autumn (see *Nature* 233, 84; 1972), is intended to provide better information to both employers and prospective graduate employees about what jobs and which people are available. Every student will get a list of the 20 most likely jobs from the computer and every employer will get a list of up to 50 potential recruits.

The scheme is not dissimilar to a computer placing system that has been operating in the United States for some years, and details of which were given to appointments officers at SCUAS's meeting last September. It is claimed that the system should encourage com-

panies who have not employed graduates before to do so and should help the student to clarify his or her ideas. It is not intended, however, that CAP will replace any part of the university appointments procedure as it now exists, it is intended simply to augment it.

The operation starts with the employer who describes the job he has to offer under seven separate headings; a job profile is produced from this at the Bootle computer centre of the Post Office National Data Processing Service and a list of profiles is sent to the appointments boards. Students consult the list and fill in forms containing the same seven headings as the employers used and these are matched by the computer against the jobs. Employers and students each receive the results and the employer may then contact applicants through the appointments boards.

It is claimed that the scheme—which has the blessing of appointments boards, the National Union of Students and employers alike—is completely confidential. Students names will not be disclosed to employers without the student's permission and use of the scheme implies no obligation on the part of students.

Included among the employers taking part are the Civil Service Commission, the armed forces, nationalized industries and private companies: the customers to start with will include the Universities of Oxford, Manchester, Kent, Sussex and Wales and Lancaster Polytechnic as well.

WATER STORAGE

Walls in the Wash

THE next stage in the Water Resources Board's plan to obtain fresh water from the Wash was launched this week with the signing of a contract to build £200,000 worth of trial embankment in the estuary.

Sir Robert McAlpine and Sons is expected to sign the contract for the work during this week. The scheme is intended to produce 100 million gallons of water a day by the end of this century and between 500 and 600 million gallons a day eventually.

Work is scheduled to start next month to see if the seabed in the Wash will form a suitable foundation for the 8 km of wall that the first reservoir will require. The walls when completed will be about 14 m high and the trial embankment will have a crest 60 m long and a base length of 160 m. The site chosen is at Breast Sand near King's Lynn.

The embankment is the beginning of a series of tests and construction trials that will cost £1.6 million over the next few years. This will eventually decide whether the walls will be able to withstand the tidal range encountered in the Wash, much larger than the range where estuary schemes have been built before. The tests will also help to determine the economics of the various methods of construction available.

ENVIRONMENT

Will the Polluter Pay?

"THE polluter must pay" is a political slogan and in practice the cost of keeping the environment clean must fall on the consumer, according to Mr A. I. Biggs of the Confederation of British Industry. Mr Biggs was one of the contributors to a one day conference on industry and the environment, organized by *The Engineer* and held on Monday of this week.

Mr Biggs pointed out that this statement was at variance with policy on pollution problems in the United States. The Americans, said Mr Biggs, have opted for a pollution tax to force polluters to consider the environment, but in Britain most of the pollution comes from the general public—for example people who own motor cars—and such a policy in Britain would not pay dividends. In particular it would be easier for any company in a monopoly position to pay the tax rather than cut down on pollution. The CBI, according to Mr Biggs, thinks "that pollution control should be considered as part of production costs".

Mr Biggs was not alone in making unfavourable comparisons of the way

in which Britain and the United States are attacking pollution problems. Mr Peter Walker, Secretary of State for the Environment, delivered the opening address at the conference, and said that Britain would be spending £850 million in the next five years on sewerage plants but that Europe and the United States were lagging behind in this essential field. He also called for a pooling of research knowledge on pollution to avoid duplication and to achieve uniform standards.

Lord Byers, in his role as director of Rio Tinto Zinc, pointed out that the anti-trust laws in the United States were a barrier to the international pooling of knowledge, and he said that there was a need for the United States to look closer at its laws relating to anti-trust matters. Dr Alan Mencher, Scientific Attaché at the United States Embassy, said that these laws were being considered at present and, although he did not give a detailed defence of the position of the United States on the various issues raised, he did point out that the audience would not be gathered together to discuss problems of the environment if the United States had not "developed a political awareness of pollution" and had not given the subject a great deal of publicity.

Sir Alan Cottrell, Chief Scientific Adviser to the government, expounded on the role of government science in the care of the environment. He mentioned several well known problems—for example, DDT, and mercury in fish—and pointed out that research was needed to obtain reliable data with which the dangers could be properly evaluated. Research was necessary, said Sir Alan, to replace the guesswork evident in documents such as the *Blueprint for Survival* and *The Limits to Growth*.

Mr C. J. Moorehouse, representing Shell, expanded on Mr Walter's theme that it was essential that uniform standards of pollution be set in all countries. In particular Mr Moorehouse was concerned at the prospect of countries setting independent standards for lead emission from cars. Mr Moorehouse said that the standards should be set by the OECD or the EEC. In another attack on legislation in the United States Mr Moorehouse said that the way in which pressure is being put on the automobile manufacturers and the oil industry to produce cars conforming to rigorous emission standards within a certain time is wrong. According to Mr Moorehouse there would be a four-year delay in producing lead-free petrol if the British government asked for it, the final product would be more expensive than petrol including lead, and would also be less economical to use in a car. Mr Moorehouse added that

the European countries "must not slavishly follow the United States's pattern" in setting emission regulations. He also pointed out that the "oil industry is in business to provide what society requires".

Mr L. Brook, chairman of Simon Engineering Ltd, approached reality when he said that what has to be decided is the "degree of pollution which is acceptable to life". He emphasized that if different countries set different standards then a tax credit system would have to be instituted to ensure that British companies are not at a disadvantage.

Although many of the participants professed that the conference had been informative and a great help to them, the basic question of whether or not the gross national product should continue to grow to the detriment of the environment was studiously avoided. But there was an overwhelming consensus among the industrialists that the cost of any improvements in processes that might be necessary to preserve the environment must be passed on to the public.

STOCKHOLM CONFERENCE

Almost Ready to Go

LAST week Mr Peter Walker, Secretary of State for the Environment, waved aloft the government's white glossy paper entitled *The Human Environment: the British View* and set the ball rolling for Stockholm. No doubt reams of newspaper comment and report are to follow, but the British government has kept its contributions reasonably compact.

The British View (HMSO, £1.20), in spite of a tendency to read like a party political broadcast, does give a careful and balanced picture of the environmental problems that Britain faces and is trying to solve. It casts its net fairly wide, including chapters on housing, local government, transport and architectural conservation, as well as the more obvious areas of pollution and depletion of resources. Interspersed among the pretty pictures and proclamations of progress there are, however, a few home truths. Ninety-one thousand acres of land in Britain are so polluted that they are useless without treatment, and as many more are in a "substandard condition". Attempts to solve the regional development problems in Britain "have met with limited success, but it would be idle to pretend that the answer has yet been found". Vehicle exhausts, the report says, are still a problem, Britain still has 2,000 miles of badly polluted rivers, and the discharge of 200,000 tonnes of polluting chemicals and heavy metals from industry into the ambient

environment "needs to be urgently controlled".

So what does the government hope to get out of Stockholm? Three things, the report says. First, a serious and balanced debate about some highly emotive environmental questions—must unrestricted growth produce famine and disease? Should there be a world population policy? Second, the government hopes to see "significant progress towards international cooperation". And third, progress towards a better use of the United Nations to deal with environmental problems.

The government is, however, opposed to the creation of a special United Nations agency for the environment. The subject is too broad, and to concentrate all environmental matters in one agency would be detrimental to the ones that already exist. The government does, however, advocate that a commission of ECOSOC should be set up to steer and coordinate the work of existing agencies and to convene inter-governmental working parties to examine areas of special concern—monitoring marine pollution, for example.

In conclusion, the government blows the trumpet of economic growth ("Economic growth . . . is indispensable. We reject the idea that solutions are to be found in the creation of less wealth") but on a muted note ("Rather we need to create more of the right kind of wealth and to use it more wisely . . .").

At Stockholm the government says it aims to "get down to brass tacks". Sweeping declarations do not cure pollution, "doing what is needed to protect the environment in the end nearly always comes down to hard slogging, unglamorous details and painstaking administration".

But behind the government's forty-two page public relations piece there lies more literature on Britain's attitudes.

Britain's views have already been tabulated once and sent to the UN which has considered them along with the views of all the other nations involved to produce the 800 pages of conference papers published last month. Then there are the background papers for the British delegation itself, not for publication. And finally there are the reports of the four working parties which Mr Peter Walker established in February 1971 to sound out public opinion on environmental questions.

The first of these, under the chairmanship of Mr R. B. Verney, published its report last week, to be followed by the other three during the next fortnight. *Sinews for Survival* (HMSO, £1), not surprisingly, treads less carefully and with more brute honesty than the official British view. It contains

no less than 53 recommendations starting off with the recommendation that Britain must have a policy to produce population stability, the first step being to publicize the facts and dangers of population growth and to provide a "free and comprehensive service in family planning".

The report says that there is a growing apprehension in Britain that the rate at which resources are being consumed is putting mankind's future in jeopardy. It says that the way resources are used in Britain is wasteful and also damaging to the environment. These concerns are reflected in the working party's fourth recommendation that "a way of defining economic growth is needed that places emphasis on quality and usefulness rather than on quantity".

The working party is concerned that the Stockholm conference will only give the population question passing attention and it calls for a United Nations conference to discuss population limitation soon after Stockholm.

Agriculture, which occupies 80 per cent of British land, with a gross output of £2,500 million and an annual expenditure of £1,300 million, must stand high in any study of resources, the report says. Whereas the working party is delighted at agriculture's increased productivity—an increase of 70 per cent in the past 20 years with the labour force decreasing by 54 per cent in that time—it is very concerned about the use of pesticides. It condemns their overuse and calls for more research into alternatives for organo-chlorine pesticides which will not damage the environment.

CHEMICAL INDUSTRY

Sharing the future

BRITAIN'S chemical industry is urged to interexchange more information on investment planning, in a report published this week. The industry's efforts to improve its forecasting must also be encouraged so that its chief immediate problem—excess capacity—can be overcome.

These are two of the recommendations to emerge from the report of the National Economic Development Committee for Chemicals (NEDO £0.85). The report runs through the past history of the industry from the halcyon days of the 1960s when it grew at a rate of 7 per cent a year (although this was a considerably lower growth rate than was managed by its foreign rivals) to last year when the growth rate dropped to less than 0.5 per cent during the year ending September 1971.

The report attempts to pinpoint the causes of this decline and to project the future of the industry.

Among the causes for the decline is a cutback in investment. Although investment in the chemical industry during the 1960s made up 15 per cent of manufacturing industry's total investment, the rate of increase was cyclical and not steady; the industry was subject to four year cycles, culminating in 1970 with the highest ever investment level of £381 million. It is predicted, however, that this will fall to £376 million in 1973—below the 1969 level (at constant prices).

The primary reason for the cutback in investment is overcapacity, according to the report. Given this situation, coupled with high inflation in the past two years (and the chemical industry, with capital costs forming a relatively high proportion of total costs, is particularly vulnerable to sudden inflation), the little Neddy constructed a computer based financial model to help predict the industry's chances of overcoming its comparative slump.

The computer runs allowed various levels of growth in the many sectors of the industry and the conclusion is that the most likely trends, based on an assumed 3 per cent growth in the GDP, are "financially just viable". This assumes a growth in output in the industry of 6.5 per cent, an increase of 6 per cent in the cost of materials and services, of 7 per cent in installed cost of plant, of 9 per cent in wages, of 5 per cent in productivity and of 6 per cent in manufacturers' prices. The return on capital from this situation, the report says, is "satisfactory", with an implied level of capital investment in 1978 of just under £1,000 million (at current prices)—a considerable improvement on the £376 million predicted for 1973: in fact, as the report puts it, it is "in all a healthy picture".

The NEDC report says that all this can happen if the assumptions about increases in costs and prices are right and provided the 6.5 per cent growth rate is achieved.

But to achieve this the industry needs better exchange of information on investment planning. "There are" the report says, "at present no restrictions on the exchange of information on investment planning" and the government should welcome the exchange. The government should also recognize the international scale on which chemical companies operate when devising and applying regulations governing monopolies and restrictive practices.

The little Neddy is also at pains to point out that the industry needs to allow for inflation to a far greater extent in its accounting procedures than it has in the past, as well as finding a better way of predicting future demand.

NEW WORLD

Alaska Pipeline Jumps the Gun

by our Washington Correspondent

SECRETARY of Interior Rogers C. B. Morton has acted with unseemly haste in deciding to grant right of way permits for construction of the trans-Alaska pipeline. After two years of study and publication of a massive report on the environmental impact on the proposed pipeline, such a charge may seem wildly exaggerated but it is being made by environmentalist organizations with some justification. And they have again gone to court in an attempt to stop the pipeline from being built.

Morton's decision to grant permits for building the pipeline was made last week, some seven and a half weeks after the Department of Interior issued its nine-volume report on the environmental and economic impacts of the proposed pipeline (see *Nature*, 236, 195; 1972). But environmentalist groups are particularly irked because the decision came only a few days after they delivered to Morton a lengthy and comprehensive critique of the impact report; they believe that the Department of Interior either rejected the arguments contained in the report out of hand or gave them only cursory examination. And the environmentalist groups are also annoyed that no public hearings have been held on the final environmental impact statement, in spite of the fact that it contained much new information and new economic arguments. Public hearings were, in fact, ruled out by William T. Pecora, Under Secretary of Interior, who called them a "circus", which would interfere with rational and thoughtful analysis.

Such sentiments would have been more palatable to environmentalist groups if the Department of Interior had facilitated rational and thoughtful analysis of the report. But in fact, only 600 copies were printed, it took weeks for orders to be delivered, only seven copies were made available by the department for public inspection in the lower 48 states, and only 45 days were allowed for scrutiny of the report's 4,600 pages and analyses to reach the department. In the event, it was the three environmental organizations involved in litigation over the pipeline—the Environmental Defense Fund, the Wilderness Society and Friends of the Earth—which assumed the chief responsibility for duplicating the report and sending it out to interested scientists and economists for comments. This situation has led the groups to accuse Morton

of default and of seeming "to discourage public contributions to the decision making process".

Why, in any case, did Morton leave himself wide open to charges of forcing a decision through without giving opponents of the pipeline a chance to make their views heard in public and without, it seems, giving more than passing notice to the lengthy critique of the environmental impact statement delivered to him only days before he announced his decision? The answer, on his own admission, is that the pipeline offers the speediest way of bringing Alaskan oil to markets, and the haste is justified by that all-embracing term national security.

In a four-page statement accompanying his decision, Morton argued that the pipeline has been subjected to a searching environmental enquiry and that "no other pipeline or petroleum transportation system is subject to the degree of protection that our stipulations will provide". But the chief justification for pressing ahead with construction of the pipeline lies in the fact that by 1980 it is estimated that demand for oil in the United States will be running at about 20 to 25 million barrels a day, while domestic production will amount to only about 9 to 12 million barrels a day. The argument is that because about half the deficit by that time will come from Arab sources which have never been particularly friendly to the United States, Alaskan oil will be needed to offset some of this reliance on potentially insecure supplies. Morton therefore concludes that "I am confident that my decision now in favour of a Trans-Alaska pipeline is in the best interests of the Nation and the American people".

But the Environmental Defense Fund, the Wilderness Society and Friends of the Earth disagree. Their report on the Department of Interior's environmental impact statement contains analyses which lead them to suggest that a pipeline built across Canada, which would deliver both oil and natural gas from Alaska and from Canadian oilfields in the Northwest Territories to the US mid-west, would offer not only environmental advantages but would also be a better proposition in terms of economics and national security. At the very least, the environmentalist groups argue, Morton should have delayed a decision on the trans-Alaska pipeline until the trans-Canada route had been subjected to a searching evaluation.

The environmentalists' report is a col-

lection of analyses prepared by independent scientists and economists who do not necessarily agree with all the views of the three groups. In many cases, however, the three environmentalist organizations were the only source through which copies of the Department of Interior's environmental impact statement was available. Nevertheless, in spite of the fact that the analyses were prepared separately, a common theme running through them is that the impact statement fails to take into account likely savings in terms of cost and environmental effects of constructing a combined gas and oil corridor. The argument which continually crops up is that because an oil pipeline must be built to transport natural gas from the North Slope oil fields—Alaskan laws do not permit it to be burned at the wellhead and although it can be injected back into the wells for a short time, that option would soon be exhausted—would it not be sensible to minimize environmental damage by building oil and gas lines alongside each other, and at the same time?

Moreover, the Department of Interior's impact statement itself points out that a route across Canada would be more desirable for a gas line because of difficulties in building a liquefaction plant at Valdez; the ice-free port at the end of the proposed trans-Alaska pipeline, and that natural gas from the Canadian fields will eventually require a pipeline to be built from the Northwest Territories, down the Mackenzie River valley to Edmonton. As an extra argument against the marine transportation route, Professor Edward Wenk together with three colleagues from the University of Washington and Dr Eugene L. Cronin of the University of Maryland, point out that there are no US harbours capable of handling the nine 250,000 ton tankers that will be used to carry oil from Valdez. What will be the environmental consequences of constructing such facilities?

But, since Morton has argued that economic and national security considerations require that North Slope oil should be brought to market as soon as possible, the environmentalists' analysis of these arguments bears some consideration. The department's impact statement itself points out that the trans-Canada pipeline and the trans-Alaska route would be equally efficient, but because the Canadian route would deliver oil to market some 3 to 5 years later than the Alaskan route, the balance is tipped strongly in favour of the latter.

That conclusion is, however, challenged on economic grounds by several contributors to the environmentalists' case.

Dr Charles J. Ciccetti and Dr John V. Krutilla, members of the staff of Resources for the Future Inc., for example, argue that differences in prices and demand for oil between the East and Midwest on the one hand and the West Coast on the other, tip the balance in favour of the Canadian route. The trans-Canada pipeline would deliver oil directly to the markets where it is most needed rather than to the West Coast, where an initial surplus could even be created by the influx of Alaskan oil, they argue. Their analysis of the impact statement suggests that the Department of Interior had used incorrect assumptions about the refinery process to be used on Alaskan crude oil, that there were inconsistencies in the derivation of oil prices in the midwest markets and that market imbalances were not taken into account.

As for national security considerations, the department's impact statement suggests that the sooner Alaskan oil is brought to market, the better it will be for national security because it would reduce US reliance on potentially insecure Arab sources. But Mr S. David Freeman, former energy policy advisor to both President Johnson and to President Nixon, believes that the issue is not quite that simple. He argues, along with Dr Richard B. Mancke of the University of Michigan and Thomas B. Stoel of the Natural Resources Defense Council, that the period between 1980 and 1985 will be more critical for national security because it has been estimated that during that period non-Canadian oil imports into the US would climb from 38 per cent to more than 50 per cent of total US consumption. Before 1980, Freeman argues that any realistic threat to oil supplies could be offset by increased domestic production and imports from secure sources.

Freeman argues that the best policy would be to encourage development of other known, secure supplies of crude oil such as the Canadian deposits in the Northwest Territories. Building the trans-Alaska pipeline would clearly not encourage such development because it would be routed away from the Canadian deposits, whereas a pipeline routed from the North Slope through the Mackenzie Valley would help stimulate production of oil in the Canadian Arctic. Moreover, it is argued several times in the environmentalists' report that the benefits to national security that derive from pressing ahead with the trans-Alaska pipeline can be realized, even if a decision were delayed, by increasing the quota of oil imported from Canada. Only last month, for example, Donald Macdonald, Canada's Minister of Energy, Mines and Resources, told

Mr Morton that the Canadian government is prepared to supply additional quantities of oil to the United States while the route is under study.

Although the environmentalist groups' report has turned out to be something of a *post mortem* on Mr Morton's decision to grant permits for the trans-Alaska pipeline, the arguments it contains will undoubtedly be raised in court. The day after the decision was announced, the Environmental Defense Fund, the Wilderness Society and Friends of the Earth, filed suit in federal court asking for a permanent injunction against construction of the pipeline. The organizations intend to pursue their case to the Supreme Court if necessary.

SHUTTLE

A Successful Launching

by our Washington Correspondent

THE space shuttle has overcome its second Congressional hurdle with considerable ease, and it should now survive the rest of the budget process with little difficulty. Last week's hurdle was approval by the Senate of the authorization bill for NASA, when powerful opponents of the project including Edmund Muskie, majority leader Mike Mansfield, Walter Mondale and William Proxmire lined up in support of an amendment to delete funding for the shuttle from NASA's budget. The move to shoot down the shuttle was, however, defeated by 61 votes to 21 and since a similar attempt in the House of Representatives failed even more ignominiously, there seems to be no prospect that anti-shuttle forces in Congress will be able to make a dent in the project when appropriations bills come up for acceptance.

The Senate's approval for the shuttle came on the same day that the Federation of American Scientists, a small but intellectually heavyweight group of scientists who lobbies chiefly for arms control, released a bruising critique of the arguments used by NASA to justify the project, prepared by Dr George W. Rathjens of MIT and Dr Von Eshelman of Stanford University.

The basis for the attack on NASA's cost estimates for the shuttle lies in the estimates for the total payload that the vehicle will place in orbit each year. According to the space agency, each launch with the shuttle will cost \$10.5 million, and the cost of delivering payloads into near Earth orbit will be reduced from \$1,000 to \$160 per pound. Rathjens and Eshelman point out that the figure of \$160 per pound is derived simply by dividing total launch costs of \$10.5 million by the maximum payload capacity of the shuttle, which is 65,000 pounds, but they contend that "there is not the slightest basis" for as-

suming that the shuttle will carry a full payload on each flight. A more realistic estimate, FAS report suggests, would be 5,000 pounds per flight, a figure which would result in launch costs of \$2,000 per pound, or double present launch costs. And these figures take no account of the research and development costs of the shuttle itself. If development costs are included, Rathjens and Eshelman suggest, launch costs would be doubled.

The FAS study therefore comes to the conclusion that "talk of reducing transportation costs by an order of magnitude through the use of the shuttle is irresponsible". Real economies in transport can be realised, Rathjens and Eshelman argue, only if the intention is to expand the manned space flight programme or the military space programme—which generally requires heavy satellites to be placed in geosynchronous orbits. "If the former is envisaged, that is the question the country should be debating, not whether to build the shuttle", the FAS report tartly suggests. On the other hand, if the idea is to increase the military space programme, then "the Department of Defense and not NASA should be paying the bulk of the costs and defending the shuttle programme".

Rathjens and Eshelman base their suggestion that the shuttle will carry an average payload of 5,000 pounds on a study carried out for NASA by Mathematica Inc., and on the fact that in 1969, a productive year in space, the total weight of scientific and applications satellites excluding Apollo launches, was only 11,400 pounds. For a full payload on each of the 30 to 50 launches that NASA is predicting each year, the total shuttle-launched payload would amount to between 1.8 and 3.2 million pounds a year, a figure that is so much greater than present launch rates that it would represent a radically different type of space programme.

The FAS study therefore concludes that the cost estimates that are challenged are peripheral to the main issue, which is "the question of the kind of space programme the country wants and should have". Rathjens and Eshelman are fearful that once built, the shuttle will be used to justify launching payloads that may otherwise not be considered, and that it will be used to maintain the momentum of the manned space programme. "The true case for the shuttle, if there is one", the study concludes, "is in manned flight (or in military programmes). To play down these aspects of the shuttle, as has been done, and to attempt to sell it as a cost-effective instrument for a civil programme to be dominated by unmanned missions involving only modest levels of public expenditures is to mislead."

Dr Vinod Shah's Protest by Suicide

New Delhi, May 12

YET another bout of heart-searching about the methods by which scientists are promoted to senior posts within the Indian government service has been triggered off by the suicide last week of Dr Vinod H. Shah, an agronomist at the Indian Agricultural Research Institute (see page 123). In a long suicide note addressed to Dr M. S. Swaminathan, Dr Shah says that he has sacrificed his "life in disgust so that other scientists may get proper treatment". Dr Shah, who was 35, had been trained at the University of Wisconsin in the 1950s, and specialized in maize agronomy. Since his return to India in 1960, he worked first for the Rockefeller Foundation and then for the Indian Agricultural Research Institute. At the time of his death, Dr Shah was Principal Investigator and Associate Project Coordinator of the Maize Improvement Scheme at the agricultural research institute.

The immediate cause of Dr Shah's grievance was that he had not been appointed to either of two senior posts in agronomy which have been filled in the past few weeks by people Dr Shah considered to be less well qualified than himself.

In his suicide note, Dr Shah complains that Dr Rajendra Prasad, recently appointed Professor of Agronomy at the Indian Agricultural Research Institute, is not qualified as an agronomist but as a soil scientist. Similarly, Dr Shah says that the new head of the Division of Agronomy at the Agricultural Research Council, Dr Rajat De, is a plant physiologist and not an agronomist.

One of Dr Shah's complaints is that it is unfair that people like himself with formal qualifications in agronomy should be passed over while scientists qualified in other fields should get the jobs. The official rejoinder is that agronomy is eminently an ill-defined discipline to which scientists with all kinds of other qualifications may usefully contribute. And in any case, it is said, there are agronomists and agronomists.

Dr Shah's letter goes on to complain that in the present organization of the agricultural research organizations, it is customary for senior people to suppress their subordinates by depriving them of research students or technical assistants, and he says that he has himself been dealt with in this way. He also com-

plains that administrative bottlenecks are many and often humiliating. The Director or Director-General seldom likes to hear complaints against the head of a division or a professor. Mediocre people are also recruited in preference to candidates with experience, energy and drive because they have the tact to keep the authorities close to them by fair or foul means.

The suicide letter also complains that Dr Swaminathan has in the past few years been presented with "a lot of unscientific data" chosen deliberately to "fit in [with] your line of thinking". He mentions specifically advice on the use of potatoes in a new crop-rotation plan being designed to produce four crops a year and the development of fertilizers from which nitrogen is released only slowly.

The issue of Dr Shah's suicide has this week been taken up in the Rajya Sabha (the Indian House of Commons) by members of both the Congress Party and the Parliamentary Opposition. On Tuesday Mr F. A. Ahmed, the Minister of Agriculture, resisted a demand that there should be a parliamentary inquiry into personnel relations at the agricultural research organizations, and threw a cat among the pigeons by making public the names of the members of the two selection committees responsible for the appointments of Drs De and Prasad. One immediate result will no doubt be to increase the difficulty of recruiting scientists to these invidious positions. Dr Swaminathan, who became Director-General of the Agricultural Research Council only three months ago, and who has retained his post as Director of the research institute pending the appointment of a successor, says that in neither case was he personally a member of the selection committees, and that in both cases he felt no reason to recommend to the Minister of Agriculture that the choices which the committees had made should be set aside.

The demand for a parliamentary inquiry is an echo of the occasion in June 1968 when the Government of India was compelled by political pressure to set up a committee of inquiry into the affairs of the Council for Scientific and Industrial Research under Mr A. K. Sarkar, a retired Supreme Judge of the High Court, but with representation from both the Rajya Sabha and the scientific community. Ironically, Dr Swaminathan was himself a member of the Sarkar Committee, which even-

tually (in 1970) produced a report which vindicated the CSIR of most of the charges of irregularities in the making of appointments. On this occasion, Mr Ahmed said that he would remit the question of Dr Shah's suicide, and the complaints in his suicide note, to an international committee of the Council for Agricultural Research, which is already considering organizational problems that have arisen within the agricultural research organizations.

Whether Dr Shah's suicide will turn out to be, as he intended, a starting point for the reconstruction of personnel policies within the government's research organizations remains to be seen.

Indeed, one of the obvious difficulties is that some of Dr Shah's complaints rest on the premise that he had been denied his rights because the authorities have not paid enough attention to the principles that appointments should be determined by a consideration of the formal qualifications of the candidates who offer themselves for senior appointments. On balance, however, there is good reason to think that the formality and inflexibility of present arrangements for making senior appointments are the most important obstacles to the more efficient organization of publicly supported research in India.

Another unfortunate consequence of the affair is that it will strengthen the unhappy tradition in which the internal affairs of supposedly autonomous research organizations become political footballs. The fact that Dr Swaminathan, a distinguished scientist who has played a monumental part in the success of Indian agricultural research in the past few years, has been personally exposed to political attacks will in the long run be a great misfortune, whatever the rights and wrongs of Dr Shah's complaints. There may be much in Indian science that needs changing to meet Dr Shah's complaints about unethical suppression of young scientists by their seniors, about the difficulty of obtaining the official ear when grievances need airing and about the preference given to mediocre scientists who are prepared to toe a professorial line, if his complaints prove to be well founded, but it will be sad if the reputation and authority of Dr Swaminathan is unnecessarily and unjustly damaged in the process when he has only just become the head of the organization against which those complaints are made.

NEWS AND VIEWS

Living Coelacanth caught off the Comoros

THE opportunity to observe a living coelacanth has occurred rarely. Indeed most of the seventy or so specimens of *Latimeria* which have become available for study since the first coelacanth was caught in 1939 have been dead for some time before preservation. The recent Franco-British-American expedition to the Comoro Islands off Madagascar was, however, more fortunate than most in that at the very end of its stay it was rewarded by the capture by a local fisherman of a coelacanth which lived for some hours afterwards.

The modern coelacanth is the closest fish relative of land vertebrates living today so that the observations made on this latest capture by N. A. Locket and R. W. Griffith (see page 175 of this issue of *Nature*) are naturally of some interest. In the conditions in which this fish was observed its swimming movements were slow and largely effected by the second dorsal and anal fins, with the pectorals playing a small part. In view of the peculiar structure of these vertical fins which are mounted on pedicles, appearing limb-like superficially (see figure), it is not perhaps surprising that when used in swimming movements their mode of action differs from analogous fins in bony fishes.

The general impression of the swimming movements of a *Latimeria* is one of unhurried motion. One of the characteristics of the living coelacanth, however, is its remarkably oily texture, its flesh, skin, and bone being heavily loaded with oil. It would not be surprising therefore to find that *Latimeria* is nearly neutrally buoyant, as has recently been demonstrated by Bone for the castor oil fish, *Ruvettus pretiosus* (Copeia, 1972; 78), and thus rarely needs to do more than wave its fins for precise orientation.

It would, however, be presuming too much to assume that this is how the coelacanth behaves in its normal habitat. It possesses a powerful axial musculature and broad tail. It must be presumed that when needed these are used in much the same way as other fish tails, to attain a sprint, away from danger, towards food, or whatever other urgent needs a coelacanth experiences. Perhaps not surprisingly, the specimen caught in the Comoros showed no sign of such action, for it had been hauled unceremoniously to the surface, then imprisoned in a cage in warm shallow water, and was finally sub-

jected to bright sunlight. The observations made have therefore to be treated with some caution and, interesting as they are, have not the same value as those that it is hoped will one day be made on coelacanths in more normal circumstances.—From our Marine Vertebrate Correspondent.

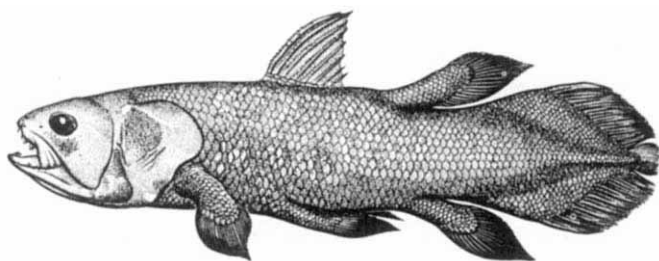
Offbeat Oxides

ELECTRON microscopy of thin films has been applied with great thoroughness to the study of defects in metal crystals: networks of dislocations, extended dislocations and extensive stacking faults are all very familiar sights to the metallurgists and physicists who have developed this tool. Metallic stacking faults are believed by some people to attract appropriate solute atoms, creating localized changes of composition, but there is no assurance of this.

Structural chemists have recently been applying electron microscopy to their own ends, numerous studies of non-stoichiometric inorganic compounds, oxides in particular, have now appeared, and in 1969 an important symposium was devoted to the chemistry of extended defects in non-metallic solids. The chief difference here from metals is that electric neutrality has to be preserved both overall and locally, and this imposes special constraints on the formation of structural defects. Stacking faults thus occur only if a compound is off stoichiometry, either through the presence of "host" ions in unusual valency states or through incorporation of aliovalent impurities.

On page 151 of this issue of *Nature*, J. S. Anderson, J. M. Browne and J. L. Hutchison reveal the details of stacking defects associated with non-stoichiometry in hitherto inaccessible detail. This work was carried out in the laboratory of Professor Anderson who, almost single-handed, built up this field of study in its early stages. Niobium oxide is the material studied here: oxide structures based on Nb_2O_5 (there are polymorphous variants) are built up of rows of $[\text{NbO}_6]$ octahedra; the rows are themselves grouped to form thicker columns, 3×4 , 4×4 or 5×3 rows in cross-section. The columns are separated by stacking discontinuities, and are combined in various weaves according to the particular polymorphic form. If the oxide is contaminated with an impurity (here Sn^{4+} in one instance, MgF_2 in another) then the electrical imbalance causes planar and linear defects to be formed at which the inter-weaving of NbO_6 columns is locally altered; the stronger atoms are of necessity incorporated in these sites.

Anderson and his colleagues are able to locate and identify these defects by high-resolution electron microscopy. The cross-section of the columns is large enough (for example, $12 \times 8 \text{ \AA}$ for a 4×3 column) for individual cross-sections to be identifiable, and so the precise nature of a "weaving imperfection" can be obtained. The



The living coelacanth, *Latimeria*, a representative of the crossopterygians from which tetrapods evolved.

photographs, with their interpretations, constitute the essential and important innovation of this article.

The authors conclude by seeking to identify the mechanism by which such imperfect non-stoichiometric structures crystallize. They are unable to decide between two alternatives: either impurity atoms are swept along in front of the crystallization front until a sufficient concentration is

attained to form a planar defect with its proper complement of impurities (in effect, a form of periodic zone-refining) or a domain pattern forms at the outset and then steers both the mode of crystallization and the distribution of impurities. The new technique certainly opens up a large and intriguing field of further research.—From our Material Sciences Correspondent.

Alpha Rhythm of an Eidetiker

EIDETIC imagery catches the imagination; the subject recurs frequently, inciting both scepticism and interest. There seems to be good evidence that some people have the ability to recall visual images in great detail and that they do this by "projecting" an internal image and scanning it. It is by no means certain that this ability is qualitatively different from those used in normal visual recall, nor that it cannot be achieved by training. Furthermore, the evidence for the existence of adult eidetikers is equivocal, because experimental demonstrations have usually lacked vigorous controls, and inevitably depend on subjective reports.

For these reasons the use of Julesz patterns to screen for eidetic imagery is welcome. A Julesz pattern, in its most simple form, consists of a stereo pair of images made up of randomly arrayed black and white squares which occur with equal probability. Both members of such a pair are identical, except that part of the pattern in one is shifted an integral number of squares with respect to the same region in the other. The disparities produced can only be recognized after fusion of the two images, and give rise to a sensation of depth. The apparent depth must be seen as a result of central processing in the visual cortex, after the super-imposition of the left and right images of a stereo pair.

Stromeyer and Psotka (*Nature*, **225**, 346; 1970) presented one of a pair of Julesz patterns to a suspected eidetiker, and gave her the second image to look at some time later. The subject could recognize objects portrayed only in the disparities between the two images. This was a striking piece of evidence for the existence of at least detailed memory of texture and produced results that seemed qualitatively unlike those for normal observers. Pollen and Trachtenberg have now

recorded the alpha rhythm of the same subject during the presentation and "eidetic recall" of various pictures. The results which were published in last week's *Nature* (**237**, 109; 1972) are disappointing in the sense that they show no dramatic differences between the eidetiker and more normal subjects performing similar tasks. It is also important that some of the original experiments using the same subject were not carried out "double blind", so that it is difficult to be absolutely certain that she is qualitatively superior in her ability for detailed visual recall.

It is plain that the subject has an excellent textual memory and that alpha rhythm activity has little apparent correlation with her abilities. This is not particularly surprising because the generation mechanism, let alone the role of the alpha rhythm, is not properly understood. There was some evidence that saccadic movements were helpful to eidetic recall involving spatial localization, and Pollen and Trachtenberg speculate about high frequency content of the electroencephalogram and the subject's ability to recall textual details. Much more evidence is needed before these suggestions can be taken seriously but any attempt to quantify and to apply objective experimental techniques to such elusive but potentially fascinating phenomena is welcome.—A. D. J. R.

AMERICAN PHYSICAL SOCIETY

Nuclear Physicists Meet

from a Correspondent

AT the spring meeting of the American Physical Society which was held in Washington from April 24 to 27, a large number of the invited speakers dealt with the topic of physics and society, as has been the case at other APS meetings of the past year. There was a round

table discussion on organizing scientists for political action and the Division of the Forum on Physics and Society organized a session on the physicist and public affairs.

By far the largest group of contributed papers (approximately five hundred) was in the field of nuclear physics and this meant an average of four parallel sessions over the four-day period. There was also a special symposium on nuclear science on April 28 and 29.

Dr G. T. Hageseth (University of North Carolina, Greensboro) reported on studies he and his colleagues (a multi-disciplinary research team) have made on the effect of broad band and single frequency noise on the germination of turnip seeds in the laboratory under controlled conditions. They have found that if seeds are subjected to noise while wet, the rate at which the seeds germinate is increased by as much as 100 per cent. One possible result of the study is the concept of producing two crops in a single year while another is weed control at the time of planting of vegetable seeds.

Dr S. E. Derenzo (Lawrence Berkeley Laboratory) reported on a new technique for radiation detection which may be as useful as the well known Geiger-Muller counter. The development of this technique may open up a new field of radiation detection technology in nuclear medicine and high energy physics. Dr Derenzo pointed out that this technique departs from past ones by using a kind of amplified electrical signal that can be induced in specially purified liquid xenon through which radiation passes. This detector is significantly more sensitive to radiation than are conventional gas detectors. He and his colleagues have built two variations one of which is about ten times more accurate than conventional gas-filled detectors in pinpointing the position of charged particles.

Drs D. R. Goosman and D. E. Alburger (Brookhaven National Laboratory) described their systematic search for new isotopes the decay properties of which have not been seen. After their discovery of ^{35}Si their next objective was ^{35}P , and this was produced by way of the $^{19}\text{F} + ^{18}\text{O} \rightarrow ^{35}\text{P} + 2\text{p}$ reaction using 42 MeV ^{19}F ions from the BNL tandem Van de Graaff accelerator. It was identified from the delayed γ rays associated with the decay of the first excited state of ^{35}S reached through a β decay of the ^{35}P ground state. The information obtained thus far agrees well with the theoretical expectations for its mass and ground state spin-parity of $J^\pi = 1/2^+$.

A technique for measuring nuclear lifetimes was reported by Dr M. Maruyama (Bell Laboratories and Rutgers University). The technique, called

crystal blocking, takes advantage of the atomic lattice in a crystalline solid to provide a very short distance scale against which the very short nuclear decay times can be measured. A germanium crystal is bombarded with 5 MeV protons to produce highly excited arsenic nuclei which are knocked out of the original lattice site. The lifetime is determined by observing how far the nuclei move from their original position before they decay. Lifetimes as short as 10^{-18} have now been measured by Dr Maruyama and his colleagues.

Dr R. Madey (Kent State University) presented a possible explanation for the "streaks and flashes" of light seen by the Apollo astronauts. It was found that two processes induce visual sensations when a particle with sufficient charge interacts with the retina of the dark-adapted eye. He and his collaborator (P. S. McNulty of Clarkson College) contend that the light reported by the astronauts results from visible Čerenkov light generated by heavy nuclei. The light flash frequencies observed agree with those calculated and the variation in frequencies reported by the astronauts can be explained by differences in the individual's efficiency for detection. A nucleus stopping in or passing slowly through the retina at a speed slower than the Čerenkov threshold creates a visual sensation through "virtual" photons which are carried by the nucleus. Madey and McNulty demonstrate the distinctions by interpreting the data obtained through exposure of human volunteers to accelerator produced radiation.

PALAEOECOLOGY

Quaternary Methodology

from a Correspondent

STUDENTS of the palaeoecology of the Quaternary period have long been in the unfortunate position of possessing a large volume of quantitative data and yet having no precise system for its interpretation. Since the work of von Post early in this century there has accumulated in Europe and North America a wealth of information concerning the fossil pollen content of peats and lake sediments, yet the account of vegetational history constructed from such evidence has been based upon intuitive interpretation. At last palaeoecologists are giving serious attention to methods available for the reconstruction of past vegetation from fossil pollen and seed assemblages, as was illustrated by the theme of the symposium of the British Ecological Society held at Cambridge on April 10-12. Although entitled "Quaternary Plant Ecology", this conference was entirely devoted to the methodology involved in dealing with

data from fossil pollen and seeds.

A number of problems are involved in environmental reconstructions using fossils, including, first, the variable rates of sediment accumulation which cause difficulty in expressing fossil deposition rates in absolute terms, and, second, the relationship between such rates and the population density of the respective species in the surrounding area. Results presented at the conference suggest that considerable advances have been made in overcoming both of these problems.

One of the most complete pieces of work presented was by Dr M. Davis (University of Michigan), who has studied the absolute pollen influx of a variety of lakes in deciduous forest and mixed forest areas of Michigan, her absolute data being derived from measurements of pollen concentrations in lake sediments formed in the period since intensive agriculture began in 1830. The start of this agricultural activity is marked in lake sediments by a sudden increase in weed pollen. Total pollen influx each year since then has been of the order of 20,000 to 40,000 pollen grains per square centimetre and its specific composition varies between the different forest types in Michigan. Because the composition of these forests is well known, this work provides data on the relationship between the abundance of a tree species and its pollen representation in absolute terms.

Similarly, fossil pollen cores can be analysed to give absolute pollen influx figures for various periods in the past, sedimentation rates being provided by radiocarbon dating at fairly close intervals in the cores. These influx data can then be interpreted in the light of the modern sedimentation studies and the contemporary vegetation can be reconstructed with some accuracy.

Although this method represents a considerable improvement upon the traditional system where pollen types are expressed in percentage terms, there remain some difficulties; first, variation of pollen influx within a single lake can be as great as three-fold, depending upon water depth; second, the pollen influx figures are obtained largely from densely wooded areas. It is possible that pollen representation of a species present at the same density in woodland or in open conditions may differ considerably. This makes it difficult to extrapolate from modern conditions to those prevailing in, say, late Wisconsin times when tundra occupied these middle latitudes of North America. Thus a direct translation from absolute pollen influx to plant density is still not possible.

In spite of these drawbacks, however, this work represents a profound advance in palaeoecological techniques. When coupled with available computerized, multivariate statistical methods and with

the rapidly accumulating information on modern pollen rain in a variety of vegetation types, all of which received considerable attention at the Cambridge symposium, such techniques may provide an opportunity for a greater degree of precision in the reconstruction of Quaternary plant communities.

ZOOLOGY

Breeding Rare Species

from a Correspondent

A RECENT conference on the breeding of endangered animal species in captivity as an aid to their survival may well mark a turning point in the history of maintenance of rare animals away from their natural habitats. The conference, which was held in Jersey on May 1-3, was jointly organized by the Jersey Wildlife Preservation Trust (hon. director, Gerald Durrell) and the Fauna Preservation Society of London (chairman, Peter Scott) and attracted more than three hundred participants from many parts of the world.

The speakers provided an impressive series of contributions on the practical techniques which have been developed for maintaining and breeding individual, rare species, ranging from the Indian rhino (Dr E. Lang, director of Basle Zoological Gardens) to several species of marmoset (Mr J. Mallinson, deputy director of Jersey Zoological Park). The conference proceedings will thus provide an extremely useful reference work for anybody who is concerned with maintaining and breeding a captive colony of an endangered species. It repeatedly emerged that the past ten years have seen unprecedented progress in the development of techniques for encouraging wild animals to breed in captivity. It was therefore very appropriate that the conference should have been held in Jersey, where Gerald Durrell has laid particular stress on breeding the rare animals in his charge—with notable success.

This new trend towards successful breeding has been accompanied by a significant change in attitudes among directors of zoos and other animal collections. Whereas it was previously true that zoos were mere museums for living animals, with breeding occurring in spite of the system, it is now widely regarded as essential to ensure successful reproduction. It is no longer justifiable, or respectable, to have just one specimen of a rare species simply for display purposes, and zoos now compete amicably for outstanding achievements in the breeding of unusual species.

This change has taken place against a background of increasing concern about the conservation of rare species in their natural habitats, and zoos can no longer justify the purchase of rare

animals from the wild simply for static display purposes. Hopefully, most rare species will soon be protected from indiscriminate trapping which is at present encouraged by the financial rewards offered by some irresponsible animal dealers and collectors.

There is also the point that effective breeding of rare species in captivity will decrease the pressure on wild populations, because zoos and other institutions will be able to supply one another. Such cooperation may in some cases lead to the establishment of a captive world stock, which can be used for display and for possible return of animals to the wild. This was clearly illustrated by the impressive report on the maintenance of the world herd of Arabian oryx (the "mascot" of the Fauna Preservation Society) at Phoenix Zoo, Arizona. In this case, an imaginative management programme is gradually providing a nucleus of animals for distribution to other breeding centres, as breeding groups. If return of the Arabian oryx to its natural habitat should ever prove to be possible, the necessary stock of captive animals will be available.

The question of return to the wild raises a number of difficulties, and this theme provoked a number of criticisms. Although it is very laudable that zoos should now be breeding their rare animals, it is questionable whether this can be regarded "as an aid to their survival". In fact, Miss M. Warland (Survival Service Commission, International Union for the Conservation of Nature) implied that the participants of the conference were wasting their time. This view is probably somewhat extreme, but it is essential that conservationists should be quite clear about the practical feasibility of releasing captive colonies in the wild. The genetic consequences of this have yet to be examined in detail, and scientifically monitored pilot projects are urgently needed.

Some attempts have already been made to release rare animals in the wild, and it seems that this can be successful at least in some cases. Dr J. Kear (Wildfowl Trust, Slimbridge) reported on a programme of release of captive-bred Hawaiian goose, and Mr C. MacFarland (University of Wisconsin) showed that various species of Galapagos tortoises are now being effectively bred and released in their natural habitat areas. In both cases, the released animals seem to be holding their own in the wild, but the long-term genetic effects have yet to be determined. Attempts have even been made to release raptorial birds in the wild (P. Wayre, Norfolk Wildlife Park), but so far with only limited success.

The background to the conference was best expressed by four basic prin-

ciples which Peter Scott emphasized in his summing-up. First of all, extinction of endangered species must be prevented at all costs. If there is any chance at all that breeding in captivity may contribute to conservation, then it should be encouraged. Second, attempts should be made to release endangered species in the wild wherever feasible. Third, every attempt should be made to reduce the present drain on natural populations. Finally, there is a basic need for education. This last point is crucial, because the zoos of the world could well provide a major educational force for conservation, provided that the zoos themselves are run in a manner which is consistent with the aims of the conservation movement.

POLLUTION

Agrochemicals Approved

from a Correspondent

A COOL look at the subject of pollution and the use of chemicals in agriculture was taken at a symposium at the Polytechnic of North London on April 6 and 7, the object of the meeting being to allow balanced appraisal of agrochemicals with no emotional overtones.

A view of hard-headed realism was put by Mr H. C. Mason (National Farmers Union) and backed by Mr K. E. Hunt (Institute of Agricultural Econ-

omics, Oxford) and other speakers that increased food production is essential to meet the needs of expanding world populations, and in spite of breeding of new crop strains, population controls and suchlike this can be achieved effectively only by the careful use of agrochemicals in controlling pests and increasing yields. This was true for both underdeveloped countries, where labour is no problem but population problems are great, and for more advanced countries where commercial intensive farming has, by necessity, replaced subsistence farming.

Mr Mason pointed out that increasing the world acreage under cultivation is a solution limited by the supply of suitable land. Even good agricultural land at present under cultivation is being continually eroded away by industrial and urban development and the setting aside of conservation and recreation areas. It was an unavoidable fact that maintaining, let alone increasing, world food production will upset natural ecosystems, whether this were by intensive or extensive methods. Mr Mason suggested that loss of habitat is of greater significance than the side effects of careful agrochemical usage. He proposed that farming should be intensified yet further; more and better controlled usage of agrochemicals could then be made, leaving larger areas free for wild life conservation and human needs.

Basic Proteins and Q β RNA Replication

ALTHOUGH the single stranded RNA genomes of bacteriophage Q β and the other RNA coliphages specify only three polypeptide chains, one of which is a subunit of the Q β RNA replicase, several other host proteins are required for the replication of the RNA of these phages. Three of the four subunits of the Q β replicase, for example, are host proteins present in uninfected *Escherichia coli* cells, and, as August and his colleagues have shown, two other protein factors (factors I and II) that are specified by the host genome are required to promote the binding of the replicase to Q β plus strand RNA.

The nature of factor II has been something of a mystery, but Kuo and August report in next Wednesday's *Nature New Biology* (May 24) that several basic proteins, which constitute as much as 3 per cent of the total protein in an *E. coli* cell, possess factor II activity and promote *in vitro* the binding of the replicase to the plus strand Q β RNA. These basic *E. coli* proteins seem to be associated with ribosomes, and Kuo and August believe that they may well be ribosomal structural proteins.

Because the basic *E. coli* proteins

which possess factor II activity are rich in lysine and arginine and have similarities to the histones of eukaryotic cells, both the *E. coli* factor II proteins and histones can, for example, be phosphorylated by protein kinase from beef heart. Kuo and August tested histones for factor II activity in an *in vitro* assay and found that not only histones but also salmon sperm protamine sulphate can completely substitute for the *E. coli* basic proteins. This is an unusual finding because most nucleic acid polymerases are inhibited by histones.

Basic proteins, such as lysozyme and cytochrome *c* and synthetic poly-L-lysine, by contrast, failed to stimulate the Q β replicase. It seems, therefore, that two chief conclusions can be drawn from these observations. First, the stimulation of binding of Q β replicase to Q β RNA plus strands by histones and *E. coli* basic proteins is not simply the result of non-specific electrostatic interactions between the Q β RNA and any basic polypeptide. Second, it seems that both histones and *E. coli* basic proteins are able to organize and maintain nucleic acids in particular conformations and that the base sequence of the nucleic acid may not be crucial.

In the discussion on the pollutant effects of pesticides and fertilizers, many speakers expressed the view that the problems are often considerably exaggerated. In some cases excessive publicity and credence are given to experimental results which are still held in doubt by some scientists. Especially interesting in this respect were the doubts cast by Dr F. Moriarty (Nature Conservancy, Monks Wood Experimental Station) on widely held beliefs on accumulation of agrochemical residues through food webs.

Using organochlorine pesticides as a primary example, Dr Moriarty reviewed the present evidence for accumulation and concluded that this, in the aquatic environment certainly, is not proven. Differential concentrations in different animals seem, according to many studies, to be attributable more to the different deposition characteristics of various tissues than to diet. The exchange and transport characteristics of the body also complicate the picture. Thus high levels of organochlorine residues in carnivorous fish, for example, seem in some studies to result primarily from initially high absorption rates directly from water and easy deposition of liposoluble residues in fat reserves. Such reserves are proportionally greater than in the herbivores making up the diet, and a superficial examination of total contents without analysis of the methods of accumulation immediately suggests that accumulation is by way of the food web. Even assessing the degree of toxicity after detecting residues is difficult, because levels tend to stabilize, often without obvious deleterious effects even at high concentrations. Mobilization of fat reserves under stress and subsequent release of stored residues can give rise to an increase in effective toxicity but little is known about this.

The difficulties of assessing toxicity and the tendency towards exaggeration were further emphasized by Dr M. Sharratt (Department of Health and Social Security) in discussing the possible side effects of agrochemicals on man. He made the point that any chemical, natural or synthesized, is toxic under appropriate conditions, depending on complex relationships of concentration and exposure levels with time. A review of data on injuries to humans arising from all types of agrochemicals shows that little hazard is involved if they are properly used. For example, only minor injuries are sustained by agricultural workers, the group most obviously at risk, from agrochemicals, whereas many deaths are attributable to accidents with machinery and so forth. Thus it seems that the beneficial effects in terms of more and better food far outweigh the hazards involved, especially if people are prepared to accept much higher hazard levels in the

use of other less beneficial chemicals.

Dr Sharratt also expressed the view that agrochemical producers are fully conscious of toxicity problems and are very careful in the development and release of new products. The exhaustive testing procedures carried out on toxicity, degradability and environmental effects to ensure proper use were emphasized by several speakers.

In the concluding general discussion, Mr B. Knights (Polytechnic of Central London) suggested that the symposium seemed to lead to the conclusion that agrochemicals are essential in maintaining and expanding world food production, and that pollution problems must be discussed with this premise in mind. Although there is no room for complacency, continuous research and careful usage can reduce the risks to the lowest level compatible with the necessity for increased food production.

The discussion revealed general agreement with this summary, but it was strongly felt that undue publicity is given by the mass media to real or suspected cases of toxicity or environmental pollution. The difficulties of putting over

a more realistic and better balanced appraisal of the facts pose real problems.

METALLOPROTEINS

Methods for Metals

from our Molecular Biology Correspondent
THE sage's imperishable maxim, "Don't never prophesy unless you know", has proved its wisdom in inorganic biochemistry as elsewhere. Attempts to identify the nature of the coordination in metalloproteins from the spectroscopic characteristics have proved, where X-ray structures have become available, to have been too frequently wide of the mark. Where the metal has a visible absorption spectrum, there is commonly little resemblance to those of the known classes of coordination complexes, and the only safe inference is apt to be that there is angular distortion of the bonds. When confronted with optical spectra of such proteins therefore the more cautious and experienced inorganic chemists have plumped firmly for doubt.

Three zinc proteins have been defined

Behaviour of Rods and Rhodopsin

WORK on X-ray diffraction of retinal rods has not established with certainty the disposition of the rhodopsin molecules in the stacked disk membranes. According to one model they lie near the inner edge of the membrane, partly in contact with the interstitial water, whereas in others they are on the outer edge, floating in the membrane, with part of the molecule exposed to the surrounding water. In an article in next Wednesday's *Nature New Biology* (May 24), Dratz *et al.* report results which they regard as evidence against all such arrangements. Dratz *et al.*'s criterion for accessibility is the extent of labelling with a reactive fluorescent species, fluorescein isothiocyanate. This reacts with primary amino groups, as well as tyrosine and cysteine side chains. They find that the reagent combines copiously with lipids when the rod has been fragmented, though less so in the intact structure, which is probably protected by the outer plasma membrane. The amount of labelling reaches a constant maximum with extensive fragmentation.

At no stage, however, is there appreciable labelling of the protein. Only when the rhodopsin is extracted with non-ionic detergent do its side chains become available for reaction. In the membrane they are apparently protected by lipid hydrocarbon, rather than the charged heads, for removal of most of the lipid head groups with phospholipase C does not promote labelling, whereas if this treatment is

followed by extraction with hexane, some reactive side chains become available. Thus Dratz *et al.* suggest that the protein molecules are completely buried in the hydrocarbon interior of the membrane. The finding that anti-rhodopsin antibodies will bind to the disks is rationalized by postulating that the antigenic determinants are in the oligosaccharide chain, which is part of the rhodopsin, and may protrude from the membrane into the water outside.

In the same issue of *Nature New Biology* another article by Bownds *et al.* is concerned with ATP-dependent phosphorylation of rhodopsin *in situ*. They find that there is very little incorporation of phosphorus in the completely dark-adapted rod. With only 1 per cent of bleaching, however, there is extensive labelling. Beyond this level of bleaching there is little further increase of incorporation. For each rhodopsin molecule bleached, ten to fifty are phosphorylated, and it is possible to achieve complete phosphorylation.

The action spectrum for this reaction coincides with the absorption band of rhodopsin, indicating that the bleaching process is directly linked to the activation of kinase activity. Thus, either the opsin is itself a kinase, or it in some way causes a kinase to become activated. A change in conductance caused by sodium ions is also maximized at 1 per cent bleaching, and Bownds *et al.* conjecture that this is controlled by rhodopsin in a manner depending on the phosphorylation.

at high resolution: insulin, in which the ligands are histidines; carboxypeptidase A, in which there are three ligands from the protein, two histidine imidazoles and a carboxyl from a glutamic acid, as well as a water molecule; and carbonic anhydrase C, where the metal is similarly coordinated in a highly distorted tetrahedral arrangement by three histidines and an extraneous group, presumably water or a hydroxyl ion. In bovine insulin, the zinc ion is shared in the crystal between three different insulin molecules, and is therefore supposed to promote formation of hexamers from dimers in solution. In guinea-pig insulin, by contrast, there is no histidine.

Zimmerman, Kells and Yip (*Biochem. Biophys. Res. Commun.*, **46**, 2127; 1972) have shown that this insulin neither binds zinc to any significant extent nor associates beyond the dimer in neutral solution, as gauged by sedimentation equilibrium, when zinc is present. The molecule is nevertheless biologically active, though noticeably less so than its bovine counterpart; evidently then the zinc is not essential for its biological utilization.

Taylor and Coleman (*Proc. US Nat. Acad. Sci.*, **69**, 859; 1972) have committed themselves to a model for the binding of the metal in alkaline phosphatase of *Escherichia coli*. This is again a zinc enzyme, each of the two identical subunits requiring one atom for activity. Various other metals can be substituted for the zinc, one of which is copper. By introducing a pure copper isotope to avoid superimposition of spectral components arising from the two isotopes present in natural copper compounds, Taylor and Coleman have been able to observe nuclear superfine structure in the ESR signals. With one copper atom per subunit, the overall spectrum is of a characteristic kind, reflecting an axially symmetric disposition of ligands. When further copper is bound a second complex makes its appearance, with less symmetrical characteristics. The superfine structure in the copper lines of the first complex is assigned to splitting by ligand nitrogen nuclei.

Direct competition between copper and zinc in this kind of complex being established, it is reasonable to identify these ligands with the active centre residues. The hypothesis then is that the copper, being coordinated in axially symmetric fashion, is in the form of a square-planar complex, with three nitrogenous side chains, most probably imidazole, as ligands, together with water (as in carbonic anhydrase) as the fourth. Whether this very plausible conclusion is the right one will no doubt become apparent when the X-ray structure of the enzyme, now reportedly coming along, finally emerges.

An experimentally more elusive metal, which is important in many enzymes, is calcium. The 2 Å-resolution structure of a calcium-binding protein, carp myogen (Nockolds, Kretsinger, Coffee and Bradshaw, *ibid.*, 581), should therefore engage the interest of inorganic chemists concerned with such matters. The function of the protein is uncertain, though various physical similarities (notably in its strikingly unusual amino-acid composition, and its very low isoelectric point) to mammalian troponin A suggest that it may be the calcium-sequestering component of the relaxing system of the fish muscle.

The sequence of this protein has been substantially determined, and the chain contours are fully defined. The chain is half α -helical, though with some distortions, and the hydrophobic core is very hydrophobic indeed: of the 108 residues 28 are seen as internal, and of these only one is polar, and this, a glutamic acid, forms an ion pair with an arginine. Among the rest are eight phenylalanines, the rings clustered in zigzag manner, just as in many crystalline benzenoid compounds, seven leucines, four isoleucines and three valines. The calcium is liganded by four carboxyls from side chains, three aspartate and one glutamate, grouped together in a short segment of the sequence, the oxygens being some 2.5 Å from the calcium. The geometry is of a distorted tetrahedral kind. It is interesting to compare this with staphylococcal nuclease, in which the calcium ion is bound by three carboxylates, two from aspartic and one from glutamic acid.

Another calcium-dependent enzyme is thermolysin and Colman, Weaver and Matthews (*Biochem. Biophys. Res. Commun.*, **46**, 1999; 1972) have found

it possible to slip lanthanides into three of the four positions that the metal normally occupies. The ability of the trivalent lanthanides to substitute for calcium has been noted in several contexts, and the message of Colman *et al.* now is that they can make excellent isomorphous replacements to ease the crystallographer's burden. The one site at which the substitution fails is only 3.8 Å from another site (the only internal one), and it is surmised that the charge repulsion between two such close-lying ions would be unacceptable with the lanthanides. Carboxyl side chains are again involved as ligands.

THE EARTH

Mantle-wide Convection

from our Geomagnetism Correspondent

ONE of the more curious phenomena in current geophysics is the apparently growing feeling that some backtracking may be necessary over the question of the scale of mantle convection. When thermal convection in the mantle first came to be regarded as a viable physical mechanism for the propulsion of continents, thus rescuing continental drift from forty years' lack of support, it was envisaged in the form of large convection cells stretching from the base of the mantle to the base of the crust. In particular, this is how it was visualized by Runcorn (see, for example, *Nature*, **195**, 1248; 1962) who did more than anybody else during the early 1960s to ensure widespread acceptance of the thermal convection mechanism.

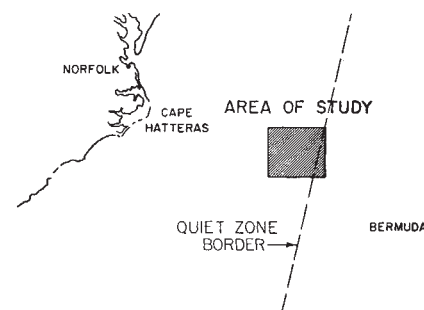
But in later years the reality of mantle-wide convection came to be questioned, though not the validity of convection itself. For one thing, the viscosity in the lower mantle seemed

Magnetic Data from the West Atlantic Quiet Zone

IN next Monday's *Nature Physical Science* (May 22), Taylor and Greenewalt, of, respectively, the US National Oceanographic Office and the Naval Research Laboratory, present magnetic data from the West Atlantic quiet zone. This zone lies just off the eastern continental margin of the United States and is some 250 km wide and about 1,500 km long. Its chief characteristic is the apparent lack of the magnetic anomalies associated with seafloor spreading.

The area which Taylor and Greenewalt selected includes, in its north-east corner, borehole number 105 of the Deep Sea Drilling Program, and in its south-east corner a region well outside the quiet zone. Taylor and Greenewalt made their measurements, both of the magnetic field at the surface of the sea and of the field further down, from a

United States naval ship while it was sailing along four predetermined tracks—two near the borehole, one in the south-east corner of the area (outside the quiet zone), and one in the north-west corner. One of the two runs near the borehole had to be abandoned because of excessive ocean currents.



too high to allow sufficient flow. Munk and MacDonald (*J. Geophys. Res.*, **65**, 2169; 1960), for example, who sought to explain the Earth's excess equatorial bulge in terms of a "fossil" bulge remaining from an Earth previously rotating more rapidly, required a viscosity of 10^{25} poises in the lower mantle.

Then, some years later, Gordon (*J. Geophys. Res.*, **70**, 2413; 1965) suggested that if the physical phenomenon which makes convection possible is diffusion creep, mantle viscosity must increase rapidly with depth. This led naturally to the idea that if mantle viscosity was going to be low enough to support convection anywhere, it would be in the upper regions. The existence of a comparatively fluid, low velocity layer in the upper mantle tied in nicely with this view; and the asthenosphere rapidly became all things to all men—most importantly, a source of magma, a natural place to look for the source of isostatic compensation, and, of course, a convenient zone within which thermal convection could be confined. Moreover, as Knopoff (*Rev. Geophys.*, **2**, 89; 1964) pointed out, if there are, as there seem to be, well defined phase changes at several depths within the upper mantle, their existence would seem to be inconsistent with penetration by large-scale convection cells.

Hitherto, any serious deviation from this general view has been restricted largely to conversations at conferences, though lately the literature has been giving the impression of leaving the options open. Thus Dicke (*J. Geophys. Res.*, **74**, 5895; 1969) has concluded, from a study of the relaxation time for a second-order harmonic distortion of the Earth, that the viscosity of the lower mantle is about 10^{22} poises; and Goldreich and Toomre (*J. Geophys. Res.*, **74**, 2555; 1969), in disagreeing with Munk and MacDonald's explanation of the excess equatorial bulge, come up with 10^{22} – 10^{24} poises for the same quantity. Moreover, Schubert *et al.* (*Science*, **169**, 1075; 1970) and Schubert and Turcotte (*J. Geophys. Res.*, **76**, 1424; 1971) have suggested that the phase change at a depth of 400 km, far from ruling out large-scale convection, may actually accentuate it. And, finally, Weertman (*Rev. Geophys.*, **8**, 145; 1970) takes the view that the physics of mantle convection is based on dislocation motion rather than diffusion creep, which will mean a smaller increase in the supposed viscosity with depth.

Now, however, Schubert and Turcotte (*J. Geophys. Res.*, **77**, 945; 1972) have made explicit the opposition to asthenospheric convection—that is, to the convection model in which the motion of the lithosphere in one direction is balanced by a return flow within the asthenosphere. The basis of

the argument is a mathematical model in which the variables depend only on depth, a simplification which is quite valid away from ridges and trenches where flow in both the lithosphere and asthenosphere must be about horizontal. The inputs to the model are the velocity of the lithosphere and the viscosity function with temperature and pressure.

This last function is unknown, although Schubert and Turcotte use a class of functions which assume the deformation mechanism to be diffusion creep (the mechanism which favours upper mantle flow) and a wide range of numerical parameters representing a range of several orders of magnitude in the viscosity. Heating by viscous dissipation is also taken into account because by increasing the temperature it decreases the viscosity, thus providing a self-lubricating mechanism. The final outputs from the model are then the heat flow due to viscous dissipation, the horizontal pressure gradient and the shear stress on the lithosphere.

What emerges in numerical terms is that, for the wide range of functions and parameters chosen, the horizontal pressure gradients lie between 0.1 and 1.0 bar km^{-1} and shear stresses in the crustal plate lie in the range 0.1 to 0.4

kb. By contrast, the surface heat flux is restricted to the very small range 0.2 – $0.3 \text{ } \mu\text{cal cm}^{-2} \text{ s}^{-1}$. But in the context of the scale of mantle convection the numerical results are less important than the qualitative consequences. Whether the force on the lithospheric plate is tension caused by a gravitational body force on the descending limb of the plate, or compression caused by gravitational sliding on the ridge flank, the return flow in the asthenosphere which balances the opposite motion of the lithosphere is driven by a hydrostatic pressure which increases with distance from the ridge. The necessary consequence of this pressure gradient is that the elevation of the ocean floor must also increase away from the ridge. Moreover, there should also be a positive gravity anomaly in the same direction.

Quite simply, neither the increase in elevation nor the positive gravity anomaly is observed. Appropriate figures suggest, for example, that the increase in elevation on the ocean floor across the Pacific from the East Pacific Rise to the Japanese trench should be about 5 km and the corresponding gravity anomaly would be 2,500 mgal. Yet observation suggests that the Pacific becomes shallower in the opposite direction; and certainly

Antigen in Human Breast Cancer Sera

THE possibility that an RNA virus analogous to the mouse mammary tumour viruses may have a role in the aetiology of breast cancer in women merits very serious consideration. In the past two years Moore and Spiegelman and their respective associates have shown not only that some human milks contain particles which in their structure and in their biochemical and biophysical parameters closely resemble the mouse mammary tumour viruses but also that polysomal RNAs present in human breast cancer cells, but not present in healthy breast cells, benign breast tumour cells or cancer cells from other organs, hybridize to a significant extent to mouse mammary tumour virus DNA.

These observations suggest that the human milk virus may be a close relative of the mouse mammary tumour viruses, that it may specifically replicate in human breast cancer cells and that it may have a role in the oncogenic transformation of breast cells. What Müller and Grossmann have to report in next Wednesday's *Nature New Biology* (May 24) certainly supports these notions.

Using a micro-double-diffusion technique, Müller and Grossmann surveyed sera taken from healthy women and from women with breast cancer for antigens which will cross-react with highly absorbed rabbit anti-mouse mammary tumour virus sera. Thirty-five

sera taken from healthy women failed completely, as expected, to cross-react with anti-mouse mammary tumour virus sera, but ten of thirty-six sera from women with breast cancer cross-reacted with three preparations of anti-mouse virus sera and the women from whom these cross-reacting sera were obtained had not had surgical treatment.

The precipitation lines with these ten human sera were completely confluent with one of the precipitation lines obtained with ether-disrupted mouse mammary tumour virus particles, and according to Müller and Grossmann there can be no doubt that the cross-reaction involving the human sera is an immunological reaction. Either, therefore, these human sera have an antigen(s) which is very similar but not identical to one of the antigens of mouse mammary tumour virus particles or the human sera have an antigen very similar to an antigen which cosediments and copurifies with the mouse virus particles.

The first of these alternatives seems by far the most probable and lends support to Charney and Moore's claim (*Nature*, **229**, 627; 1971) that sera from some women with breast cancer reduce the biological activity of mouse mammary tumour virus as well as to the idea that human breast cancer may be, at least in part, a viral disease.

such a gravity anomaly is more than an order of magnitude greater than any actually measured. And as a result, Schubert and Turcotte conclude that the physical model is wrong—that is, that the balancing flow at depth is not limited to the asthenosphere. The balancing flow must be deeper in the mantle, possibly even below 700 km “and possibly throughout the entire mantle”. The upper mantle immediately below the lithosphere must then be moving in the same, rather than opposite, direction as the lithosphere; and “it is likely that the dominant deformation mechanism is dislocation glide”. In short, earth scientists are back where they were in the early 1960s.

RIBOSOMAL RNA

Maturation Pathways

from our Cell Biology Correspondent

IF the contents of recent issues of the *Journal of Molecular Biology* are anything to judge by over the past two or three years, more than a few molecular biologists in search of a quiet but honest way of earning their living have been attracted to the question of the biosynthesis of ribosomal RNAs in eukaryotes. Quasi-repetitive research, to use the journal's own description, it may be, but much current research does not fall in that bracket and those molecular biologists who have pursued the mechanism of ribosomal RNA synthesis can at least point to a large corpus of sound information as a result of their efforts. Indeed, eukaryotic ribosomal RNAs and their precursors are almost as well characterized as their bacterial counterparts.

Maden and his associates, for example (*Nature New Biology*, 237, 5; 1972), have by fingerprint analysis unambiguously confirmed the maturation pathway of HeLa cell ribosomal RNAs proposed by Penman and his associates and others from kinetic studies. And Udem and Warner (*J. Mol. Biol.*, 65, 227; 1972), by measuring the kinetics of labelling of the short lived 35S, 27S and 20S ribosomal RNA species as well as the stable, mature 25S and 18S species in spheroplasts of the yeast *Saccharomyces cerevisiae*, have been able to draw up a maturation pathway for this species. Udem and Warner conclude that the product of transcription of the ribosomal RNA genes is a single 35S polynucleotide chain with a molecular weight of about 2.5×10^6 which on conservative cleavage yields one 27S RNA (molecular weight 1.6×10^6) and one 20S RNA (molecular weight 0.8×10^6). These molecules are in turn cleaved, with the loss of about 20 per cent of the primary product of transcription, to yield the mature 25S and 18S species

by a terminal processing step, which is sensitive to inhibition by cycloheximide and is, presumably, dependent on continuous protein synthesis. The 5.8S RNA, which is associated with the mature 25S ribosomal RNA and from which it can be released by denaturing agents, is apparently produced at the final cleavage step from the 27S precursor RNA. Ribosomal 5S RNA, by contrast, seems to be the product of independent transcription of a separate gene.

As Udem and Warner point out, these data not only support the idea that in all eukaryotes the pathway of biosynthesis of ribosomal RNAs is essentially similar but also draw attention to the advantages of *S. cerevisiae* over cultivated animal cells for the experimentalist. They emphasize this point by describing in a subsequent report (*ibid.*, 243) the isolation of mutant strains of yeast in which ribosomal RNA biosynthesis is temperature sensitive. Temperature sensitive mutations in nine genes all apparently inhibit to varying extents (50–80 per cent) the transcription of the 35S precursor RNA and the subsequent maturation of what little precursor is made. Moreover, in the three mutant strains which have been examined, the synthesis of ribosomal proteins is reduced by about 75 per cent. Because neither precursor RNAs nor defective ribosomal particles or subunits accumulate in any of these mutant strains, Warner and Udem confidently conclude that the whole process of ribosome biosynthesis in this yeast is stringently regulated by some feedback inhibition mechanism.

Stevens and Pachler (*J. Mol. Biol.*, 66, 225; 1972) contend that the low mole-

cular weight (4–6S) RNA which has been found associated by hydrogen bonds with the mature RNA of the large ribosomal subunit of some plant and animal cells is a universal and diagnostic characteristic of eukaryotic cells. Such RNA has never been found with the large ribosomal RNA of prokaryotes but, as they report, an RNA with a molecular weight of about 4.3×10^4 is liberated by denaturing agents from the 26S ribosomal RNA of the protozoan *Acanthamoeba castellanii*, a lowly eukaryote. What is more surprising, on denaturation the 26S RNA itself seems to dissociate into two molecules sedimenting at 16–18S, and Stevens and Pachler believe, therefore, that the 26S ribosomal RNA in this species comprises three RNA species with molecular weights of 0.88×10^6 , 0.6×10^6 and 4.3×10^4 , held together by hydrogen bonds.

The ribosomal RNAs of a prokaryote, the trachoma agent which is an obligate parasite of eukaryocytes, have also recently been investigated as Gutter and Becker report (*ibid.*, 239). They have identified in infected FL cells exposed to emetine which inhibits cellular RNA synthesis a 17.2S precursor of the mature 16S ribosomal RNA of trachoma agent ribosomes and suggest that the mature 23S ribosomal RNA may also be matured from a larger precursor. The maturation of the 17.2S precursor, which is a slow process, seems to be blocked by chloramphenicol and the synthesis of the precursor and its maturation is inhibited by puromycin. In short, although the trachoma agent has its idiosyncrasies, the synthesis and maturation of its ribosomal RNAs clearly follow the bacterial pattern.

Virus Infection and Cell Agglutination

WHEN cells are transformed either by RNA or by DNA tumour viruses or by chemical carcinogens their susceptibility to agglutination by plant lectins such as concanavalin A or wheat germ agglutinin is greatly increased. Burger has suggested that the changes in the cell surface consequent upon transformation which are reflected by the enhanced agglutinability may be responsible for the failure of transformed cells to respond to the molecular signals which regulate cell division. But as Poste and Reeve confirm in *Nature New Biology* next Wednesday (May 24) an increased susceptibility to agglutination by these two lectins is by no means a specific property of transformed cells.

The precise nature of the changes which cause transformed cells to be more readily agglutinated by lectins is obscure but nobody seriously doubts that they involve components of the cell coat and because many lytic, non-

oncogenic viruses are known to cause changes at the cell surface Reeve and Poste decided to compare the susceptibility to agglutination of BHK cells and chick embryo cells before and after infection with Newcastle disease virus. At the same time, in parallel experiments, Reeve and Poste measured the thickness of the cell coat with an ellipsometer.

Poste and Reeve's results indicate, first, that infection with Newcastle disease virus renders cells susceptible to agglutination by both concanavalin A and wheat germ agglutinin and, second, that as the cells become more readily agglutinable so the thickness of the cell coat decreases. When, however, cells are infected with a strain of Newcastle disease virus which replicates without altering the cell coat material the cells do not become susceptible to agglutination, neither does the cell coat layer become thinner; the two changes may therefore be related.

Evolutionary Significance of the HL-A System

W. F. BODMER

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It is still an open question how the genetic polymorphism represented by the principal human histocompatibility system is maintained. But it may have evolved as a consequence of the necessity for cell to cell recognition during development and morphogenesis.

THE HL-A system, which is usually detected as an antigenic polymorphism on lymphocytes (or platelets), seems to be the major human histocompatibility system¹⁻³. Recent evidence has focused attention on the biological role of histocompatibility antigens and on the factors controlling their evolution. Histocompatibility antigens show a remarkable degree of genetic variation and seem to be associated with a possibly large number of closely linked genes. Such genes have been shown to control differences in immune response and so differential susceptibility to infectious diseases, including tumours induced by viruses. A close interrelationship between histocompatibility genes and immunoglobulin genes has also been suggested. This report aims to try to unite these various observations and theories in a coherent picture of the evolution of major histocompatibility antigen systems, with special reference to HL-A and, at the same time, to suggest a possible role for the antigens and their associated genes in the control of cell-cell recognition during differentiation.

A genetic polymorphism is most simply defined operationally by the existence, in one population, of two or more alleles at a given locus, each of which occurs with an appreciable frequency—say, more than 1%. Histocompatibility systems are thus, by their definition, genetic polymorphisms.

One major system for the control of graft rejection has been found in all species which have been adequately studied: these systems, in mouse (H2) and in man (HL-A), are by far the most extensively studied, and are considered to be homologous. It is now generally accepted that the HL-A antigens can be separated into two major series, LA and 4, each of which behaves as if its constituent antigens were controlled by a set of alleles at a single locus⁴. Pedigree data show that the LA and 4 loci are closely linked.

Each HL-A chromosome combination, or haplotype, thus consists of one genetic determinant (or a blank) from the LA antigen series, and one from the 4 series (Table 1). The antigens of the H2 system can similarly be separated into two series, which correspond to the D and K regions of the H2 system as defined by recombination studies⁵⁻⁷. Preliminary evidence indicates a similar two-locus structure for the major histocompatibility systems of chimpanzee⁸, rhesus monkey⁹ and dog (B. Vriesdorp and R. Epstein, personal communication), suggesting that these systems may all be homologous and have a similar genetic structure. The homology of the various systems in different species is further emphasized by the observation of cross-reaction between HL-A antigens and antigens of chimpanzee, rhesus monkey, and even cattle¹⁰ and rabbit¹¹.

Table 1 HL-A Antigens of the LA and 4 Series with their Corresponding Gene Frequencies in Caucasians

LA		4	
HL-A1	0.16	HL-A5	0.06
HL-A2	0.31	HL-A7	0.12
HL-A3	0.15	HL-A8	0.09
HL-A9	0.13	HL-A12	0.13
HL-A10	0.06	HL-A13	0.02
HL-A11	0.07	W5	0.09
W19	0.06	W10	0.05
W28	0.05	W14	0.04
Blank	0.01	W15	0.06
		W17	0.04
		W18	0.06
		W22	0.03
		W27	0.04
		Blank	0.17

Based on data from the Fourth International Histocompatibility Testing Workshop⁴. The HL-A numbers are the officially recognized antigens and the W numbers refer to the provisionally identified antigens. Several new antigens not listed here have been described since the Fourth Workshop. Haplotypes are pairwise combinations which are generally inherited together, such as 1 8 and 3 7 so that a typical genotype is $\frac{1}{3} \frac{8}{7}$.

Extent of HL-A Polymorphism

The extent to which a system is polymorphic can most simply be measured by the overall frequency of heterozygotes with respect to the system: the complement of this is the overall frequency of homozygotes. Assuming random mating, the latter is merely the sum of the squares of the gene frequencies for all the alleles of the system. For example, the frequency of homozygotes in the Rh system ranges from 34% in Caucasians to 62% in Orientals, and the frequency of homozygotes for the ABO blood groups is around 50% in most populations (Table 2). By contrast, the frequency of homozygotes for just the LA locus of the HL-A system is only 18% in Caucasians, and ranges up to 33% for Guatemalan Indians which, with respect to the HL-A (and other) systems, seems to be one of the most homogeneous populations yet studied. The overall frequency of homozygotes for the 4 locus is, for most populations, even lower than that for the LA locus. The total frequency of homozygotes combining both loci of the HL-A system is therefore less than 2% for Caucasians and Africans. This indicates a remarkable level of variability for the HL-A system by comparison with other known polymorphisms.

Overall Levels of Polymorphism

The work of Lewontin and Hubby¹⁵ in *Drosophila* and Harris in man¹⁶ (subsequently extended to many other species)¹⁷ has shown that at least 30%, or possibly even more, of all gene loci may be polymorphic. The classical explanation for a balanced polymorphism is that it is caused by a selective advantage of heterozygotes over homozygotes, but it has recently been asked whether so many polymorphic genes can all be maintained by some such form of selection. The usual assumption of independent action of polymorphic loci is

Table 2 Overall Frequency of Homozygosity: Comparison of the Rh, ABO and HL-A Systems in Different Populations

	Caucasians	African blacks	Orientals	Guatemalan Indians
Rh	0.34	0.57	0.62	
ABO	0.49	0.53	0.48	
HL-A system*			Japanese	
LA locus	0.18	0.18	0.24	0.33
4 locus	0.10	0.11	0.18	0.31
Two loci combined (product)	0.018	0.019	0.044	0.1

Sources of data: (a) Rh and ABO from Cavalli-Sforza and Bodmer¹², Table 11.7, takes account of most Rh antigens and also A₁ and A₂ of the ABO system. (b) HL-A: Caucasians—Allen *et al.*⁴, Japanese—Albert *et al.*¹³; African blacks and Guatemalans—W. F. B., J. G. Bodmer, H. Cann, and C. Barnett, unpublished data.

* These figures are over-estimates because, necessarily, they do not take account of new antigens, known or yet to be discovered (see, for example, ref. 14). The higher homozygote frequency for Japanese is, for example, probably because these data are based on fewer antigens than that for the other populations. The Guatemalan Indians, on the other hand, seem to be substantially more homozygous than the other groups.

arbitrary, and severely limits the number of loci that can be kept polymorphic for a given overall level of selective elimination¹⁸⁻²⁰. Mechanisms for maintaining polymorphisms other than heterozygote advantage—such as frequency dependent selection, in which the advantage of a given genotype is inversely proportional to its frequency—do not contribute significantly to the overall level of selective elimination^{21,22}. Nevertheless, it seems hard to envisage that all polymorphisms are selectively maintained, although this may be so in an appreciable amount of the observed polymorphisms¹⁸. Many polymorphisms may, in fact, be relics of previous selective crises, and are thus no longer subject to significant selection. Linkage may also play a very important part in the maintenance of polymorphisms—relatively large numbers of neutral or almost neutral genes may be held polymorphic in a population by the effects of selection on closely linked polymorphic loci²³⁻²⁵. It may, actually, be best to think of polymorphism in terms of chromosome regions containing many genes, only some of which are subject to significant selective pressures and interactions²⁶.

Number of Genes in the HL-A Region

Given the frequency of polymorphism, the question arises whether the HL-A system is an extreme case of polymorphism or whether it simply includes many closely linked genes, each of which by itself is, at best, only moderately polymorphic. If, for example, the observed HL-A antigens reflect the activity of twenty structural genes, about half would be expected to be polymorphic for at least one alternative. This would lead to the possible existence of 2^{10} (1,024) different haplotypes, which is well in excess of the observed level of polymorphism for the HL-A system.

Data on recombination between the LA and 4 loci indicate a recombination fraction of between 0.5 and 1%, with a mean of about 0.8^{27,28}. Assuming that the average frequency of recombination in the HL-A region is the same as elsewhere in the human genome (that is, that the HL-A region is not a recombinational "hot spot"), it is possible to calculate what fraction of the total genome is represented by the HL-A region, and thus how many genes or cistrons it contains. The average observed number of chiasmata per human meiosis is about 51 (ref. 29) and so, assuming a direct relation between chiasmata and cross-overs, the total human map length is $\frac{51}{2} \times 100 = 2,550$ centimorgans. A recombination fraction of

0.8% thus represents a fraction of $\frac{0.8}{2550} = 0.0003$ of the human genome. Now the number of nucleotide pairs per human

haploid complement is approximately 3×10^9 which, assuming all the DNA to be functional and an average cistron length of 150 amino-acids or 450 nucleotide pairs, means that the human genome contains $\frac{3 \times 10^9}{450}$ or 6.7×10^6 cistrons. On this basis, the HL-A region includes $0.0003 \times 6.7 \times 10^6$ or about 2,000 cistrons.

Even allowing for appreciable redundancy in the DNA, it seems likely that the number of cistrons in the HL-A region is at least in the hundreds. The important question, however, is not so much how many genes there are between the LA and the 4 loci, but how many genes determine the expression of the LA and the 4 antigens. The apparent allelism of the genetic determinants of the antigens controlled by each of these loci by no means implies that the two series of antigens each necessarily represent the activity of a single structural gene²⁷. It seems possible, in fact, that closely related, highly cross-reacting antigens within a series, such as HL-A2 and W28 (or Ba*), may have been derived one from the other (say, W28 from HL-A2) by recombination. Thus the product of recombination between alleles of a series may partially reflect its parental origins, but is not clearly recognized as a recombinant product and behaves simply as a new antigen of the series^{27,30}. Plausible models of the biosynthesis or chemical structure of these antigens can be constructed in terms of many structural genes for each set of antigens. The answer to this puzzle will probably come from a careful study of the chemistry of the antigens. Preliminary data suggest that the product of each locus is a relatively uniform protein³¹. This, if confirmed, would argue in favour of a single structural gene for each set of antigens, and thus a unique level of polymorphism for the HL-A system.

Undoubtedly, if the HL-A antigens do reflect the activity of only two structural gene loci, the level of polymorphism for this system would suggest the existence of special selective mechanisms to maintain it. If, however, many structural gene loci are involved, then the HL-A polymorphism may pose no more of a problem than any other "average" polymorphism.

Selection in the HL-A System

The simplest and most direct evidence for selection would come from data showing departures from expected Mendelian segregation of the HL-A antigens in families. This, however, only measures selection due to viability differentials associated with different HL-A phenotypes or genotypes, and provides no information on possible fertility differentials. Data on the segregation of single HL-A antigens in backcrosses and intercrosses show no evidence of departure from the expected Mendelian proportions^{4,32}, although this might be argued to be a weak test for selection. It would not uncover disturbances associated with particular haplotypes (as opposed to single antigens) nor would it be likely to uncover incompatibility selection caused by the effects of maternal antibody on the foetus. More complex tests for departure from expected Mendelian segregation without identifying particular antigens have been devised³³, but these also show no evidence of significant departures from expectation in the absence of selection.

Foetal-Maternal Interactions

The relatively high incidence of foeto-maternal stimulation with respect to the HL-A antigens raises the possibility that they may be associated with significant incompatibility selection against the foetus. Such selection has been suggested for the ABO system, and is, of course, known to occur, to some extent, through haemolytic disease of the newborn, for the Rh system (for a review see, for example, ref. 12). Such incompatibility selection is not, however, on its own a mechanism for maintaining polymorphism. In fact, it generally acts against polymorphism, because it leads to heterozygote dis-

advantage^{12,33}. It is well known that maternal HL-A antibodies do not, in general, have any untoward effects on the foetus³⁴, and no convincing data exist indicating, for example, a higher proportion of stillbirths or abortions connected with maternal HL-A sensitization³⁵. To my knowledge, however, no comprehensive search has yet been made for fertility differences connected with different levels of HL-A incompatibility between mother and offspring, associated, for example, with the occurrence and amount of HL-A antibody in the mother.

It has been suggested that antigenic disparity between mother and foetus may actually favour the growth and survival of the foetus, rather than causing selection against it^{37,36}. This is based on data in the mouse showing that antigen differences can apparently increase the size of the placenta³⁸⁻⁴⁰ and by observations in the mouse⁴¹ and rat^{42,43}, showing significant and sometimes striking increases in the relative survival of offspring which were antigenically incompatible with their mothers. Such heterozygote advantage could, in principle, account for the maintenance of histocompatibility polymorphism. It is interesting to note, however, that in each of the cases reported so far, the principal selective effect seems to be associated either directly or indirectly with only minor histocompatibility loci. Certainly, as already mentioned, there is not yet any evidence of selection which favours or disfavors antigenic disparity with respect to the HL-A system. Kirby⁴⁴ has reviewed the problem of why the foetus is not rejected as a homograft and whether, in fact, antigenic disparity serves a purpose with respect to the development and maturation of the foetus. The most likely answer is that the foetus and mother are effectively separated from each other with respect to most of the severe immune stimuli and reactions by the layer of trophoblasts and decidual tissue which envelops the placenta.

HL-A and Disease

Another direct approach to the search for selection connected with polymorphisms such as the HL-A system is to look for associations between HL-A antigens and diseases that may be of selective significance. On the assumption that polymorphisms such as the red blood cell groups must be maintained by selection, Ford⁴⁵ urged a search for associations between blood groups and specific diseases. The idea that there might be associations between the ABO blood groups and disease must have been in Landsteiner's mind at the time he discovered them, but was discarded, or perhaps discredited, in the intervening years. Following the discovery by Aird and co-workers⁴⁶ of a significant association between blood type A and cancer of the stomach, many other significant associations have been reported. A number of these have been amply confirmed and are clearly highly significant (for review see, for example, refs. 31 and 46), but none of them is yet explicable in terms of any plausible biochemical models; and few, if any, seem to be significant with respect to natural selection. Thus, for example, it has been shown that the association between blood type O and duodenal ulcer results in fitness differences between type O and types A, B or AB as low as 1 in 10⁴ to 1 in 10⁵, which are really too small to be of much evolutionary significance¹². This is because duodenal ulcer and other diseases associated with the blood groups are rare diseases which have their effect mainly late in life after the end of the reproductive period. The search for significant selective effects of the red blood cell groups and their association with disease has been a most frustrating one, producing inconsistencies and statistical pitfalls^{47,48}. The problems of these studies should be a warning to investigators looking for associations between the HL-A polymorphism and diseases. A rationale for the existence of some such associations has, however, been provided by two important lines of investigation. First, work by McDevitt *et al.*⁴⁹ has shown that in the mouse, the guinea-pig and other animals there is a close connexion between major, and possibly also minor, histocompatibility

systems and the genetic control of the immune response. Second, studies by Lilly^{50,51} and others have provided evidence for histocompatibility-linked genetically controlled resistance to some viruses that may be carcinogenic⁵². Following the stimulus of these studies, investigators have now begun to search for associations between HL-A antigens and diseases. The first significant association, reported by Amiel⁵³, was that between Hodgkin's disease and an antigen then called 4c and now known to be a combination of HL-A5, W5 and W18⁴. This association has since been confirmed in at least two further independent studies though it is not clear which of the three antigens, HL-A5, W5 and W18, is primarily involved^{54,55}, although further evidence suggests that not all forms of Hodgkin's disease are involved in this association^{54,56}. Another highly significant association was found independently by two different groups of workers between systemic lupus erythematosus and the antigen W15 (formerly LND)^{57,58}. Other apparently significant associations have been described for some forms of leukaemia, for asthma, mononucleosis and other diseases (see, for example, refs. 59, 60, 61). The picture is complicated by heterogeneity, for example, in diseases and control populations and by statistical problems connected with the fact that the largest associations are emphasized and so ordinary significance tests, which refer to random samples, cannot properly be used to judge the associations. Nevertheless, it seems that out of the mass of data which is now rapidly being accumulated some significant associations will be established, and these may well be of great importance for understanding the genetic control of disease resistance in relation to the immune response and susceptibility to infection by viruses and other pathogens. Whether such associations will be of any significance for the selective maintenance of the HL-A polymorphism is quite a different question. Most of the diseases studied so far are very rare, or occur late in life, or have little effect on viability or fertility. It seems unlikely that any of the associations reported so far would be of much more selective significance than is the association between duodenal ulcer and blood type O. If, however, associations were found with important infectious diseases, such as smallpox or cholera, that have now, or had in the past, a relatively high incidence, then these could well be of great significance for the evolution of the HL-A system.

Resistance to Pathogens

There are at least three mechanisms other than control of the immune response that could lead to direct associations between histocompatibility antigens and resistance to pathogens. Two of these have been discussed by Snell⁶² in connexion with the mouse H2 system and virus infection. The first mechanism invokes "molecular mimicry" between histocompatibility antigens and viral antigens. Thus, if the major external antigen of a virus has the same specificity as a given HL-A antigen, then individuals carrying this particular antigen may not be able to develop an immune response to the virus, and thus may be more susceptible to infection by it. The second possibility discussed by Snell is that, given histocompatibility, antigens may act as, or interact with, receptor sites on the cell surface, for the attachment of viruses. This possibility is supported, for example, by data which associate susceptibility to an avian leucosis virus with a chick erythrocyte antigen⁶³. Both of these situations could be the consequence of evolutionary adaptation by viruses to increase their infectious efficiency. It might then be argued that it is to the advantage of a population to have as wide a variety of histocompatibility antigens as possible, to slow down the rate at which viruses can adapt to successful infection of the majority of individuals in a population. Selection at the population level is, however, notoriously ineffective and it is generally assumed that apart from sex, hardly any character has evolved by population or group selection⁶⁴. Moreover, once the viruses have adapted, those individuals which carry the most antigens, which will be

the heterozygotes, will be most susceptible to infection with different viruses. Once again, as in the case of adverse incompatibility selection due to foetal maternal interaction, this leads to selection against heterozygotes, and thus cannot account for the maintenance of polymorphism. The possibility remains, however, that individuals which carry new antigens which have arisen comparatively recently by mutation or recombination will be at an advantage because viruses will not yet have had the time or the opportunity to adapt to infecting cells carrying a new antigen. This would give rise to frequency-dependent selection, in which the less frequent genotypes are favoured, which, as has already been discussed, is known to be a mechanism that can maintain polymorphism^{21,22}.

Another selective mechanism based on preferential disease resistance which could maintain polymorphisms has been suggested by Lederberg (personal communication: see ref. 12, p. 212) and others. It is known that some viruses incorporate into their coat a portion of the membrane of the cell which they are attacking. In this way they acquire some of the host's antigens. If such a virus now attacks a person with a different antigenic constitution, the victim may respond with antibodies directed against the antigens acquired by the virus from its previous host, and may thus be better protected against the viral infection. The immune response to such "passenger" viral antigens would presumably have to be elicited by the initial incoming virus. This follows from the fact that, presumably, after a round of growth in the cells of its new host, the virus would have acquired histocompatibility antigens from this new host, and these therefore could no longer elicit an immune response. Pre-existing HL-A antibodies, for example, in multiparous women could, of course, accelerate the immune response to the initial infection. Clearly, the greater the heterogeneity in the population with respect to cell surface antigens that can become incorporated into viral coats in this way, the greater the probability that such a virus will encounter a relatively hostile immune environment. This would lead to an overall advantage of heterozygosity with respect to such antigens, and, in particular, to an advantage for new antigens, and could perhaps help to account for excessive levels of polymorphism. So far, there is no direct evidence to support the existence of such a selective mechanism against viruses. An apparent model example described by Nandi⁶⁵ can, it seems, be explained by viruses being transmitted when inside red cells⁶⁶. An electron microscopic study by Aoki *et al.*⁶⁷, of the distribution of H2 antigen on the surface of virus infected cells, indicated no H2 antigen in regions of the outer membrane where virus was leaving the cell. A study of the liver fluke, *Schistosoma mansoni*, does, however, indicate the presence of host cell surface antigens on the adult worms⁶⁸.

An analogous mechanism of selection in relation to histocompatibility polymorphisms has been discussed by Gorer⁶⁹ and Burnet⁷⁰. They suggested that these polymorphisms may have evolved to protect the individual from contagious "infection" by cancerous cells transferred directly from one individual to another. The higher the level of histocompatibility polymorphism, the higher will be the probability that such transferred cancerous cells from another random individual will be rejected. At least two examples of such contagious tumours have been described, one in dogs⁷¹ and the other in hamsters⁷². There is, however, little or no information on possible rates of infection by cancerous cells, and it seems unlikely that this could be a common phenomenon. Furthermore, most cancers occur relatively late in life and so are unlikely to be very significant for differential selection.

Variation in HL-A Gene Frequencies

A much less direct, and admittedly more complex, way of looking for selection in relation to a polymorphism is to analyse the variation in the frequencies of its constituent alleles between different populations. Gene frequency differences between populations arise by chance, leading to a given expected level

of variation in the absence of any selective pressures. Those polymorphisms which have alleles with different selective advantages in different geographical areas will tend to be more variable than the norm in the absence of selection, while those polymorphisms which have relatively constant selective values associated with their constituent alleles in different populations will be expected to be less variable than the norm. Thus, if we examine variation amongst a large number of populations with respect to a number of polymorphisms, it may be argued that the most variable polymorphisms represent differential selection against populations, the least variable represent stabilizing selection in different populations, while those in the middle range may reflect the norm of variation expected in the absence of selection (see, for example, ref. 12). The difficulty with this analysis is that it is hard using the available theory and data to set limits to the level of variation to be expected in the absence of selection. Nevertheless, it is worth mentioning that variation for the HL-A system has been shown, in a limited study, to be at the lower end of the spectrum⁷³. The HL-A variation was in fact comparable with the least variable of the previously known polymorphisms. This could be taken to be an indication that some form of stabilizing selection, namely, selection common to most populations, is involved in the maintenance of the HL-A polymorphism.

Use of Mixed Populations

Another related approach to the search for selection is to study gene frequencies in populations, such as the American blacks, which are known to be mixtures of two or more reasonably well defined populations, in this case Caucasians and African blacks. The mixture is due to a persistent, though small, level of intermixture between the original populations over some period of time. This has led to a population whose gene frequencies can be thought of as a simple mixture of those of the two populations from which it is derived. Each polymorphic system which shows differences in gene frequencies between the two parent populations, in this case Caucasians and Africans, can provide an estimate of the extent of admixture present in the mixed population, the American blacks. If, since the time the intermixture between the constituent populations started, there has been no selection with respect to the polymorphism in question, then the extent of admixture estimated from the gene frequencies should truly reflect the accumulated effect of intermixture. If, on the other hand, there has been differential selection for or against a particular allele, then this will bias, either upward or down, the estimate of admixture obtained using this allele. Consider, for example, the Hb S allele responsible for the sickle cell trait. This is thought to be maintained in Africa by an enhanced resistance of the sickle cell trait heterozygote to malaria⁷⁴. In the United States, in the absence of malaria, these heterozygotes may be at a slight disadvantage relative to the normal homozygote, resulting in selection against the Hb S allele. Thus, in one body of data analysed by Ceppellini⁷⁵ comparing blacks and whites from South Carolina, the estimates of admixture for the Rh, Duffy and Lewis systems were around 0.2 while the corresponding estimate for the Hb S gene was 0.38. A similar two-fold increase in the Caucasian admixture rate obtained from data on the Hb S allele was found in New York⁷⁵, and for the data collected by Workman *et al.*⁷⁶ in Claxton, Georgia. These results agree with the suggestion that there is selection against the Hb S allele in the United States environment, leading to an apparently higher rate of admixture with respect to this allele than for others which are presumably not subject to selection. Such a study is uncovering the cumulative effects of the seven or so generations of selection that have taken place since slaves were brought from Africa to the Americas. A similar study with respect to the HL-A system would be of great interest, for this may be a relatively efficient way to search for selection associated with any given polymorphism.

Advantage of New HL-A Antigens

If the LA and 4 series of antigens are each really produced by a single cistron, then the level of polymorphism for the HL-A system would seem to be unique, perhaps even comparable with that observed for the S allele incompatibility systems in plants. In these latter systems, any new allele is favoured by the nature of the incompatibility system (see, for example, refs. 77 and 78, pp. 104–110). Perhaps the same could be true with respect to new HL-A specificities produced by mutation or recombination. The mechanisms already suggested for association between antigen polymorphisms and diseases caused by viruses and other pathogens would lead to an advantage for any new allele. Another possible mechanism might be through HL-A antibodies which were sometimes present in the cervical mucosa or secretions and which tended to inhibit fertilization by sperm carrying the corresponding antigen. A sperm carrying a new antigen would never meet its corresponding antibody, and so might tend to be favoured³². On the assumption, however, that HL-A antibodies only occur as a result of foetal-maternal stimulation, this mechanism could only apply to the sperm which actually first carry a new mutation, and then only if the corresponding new antigen could be expressed on the sperm, all of which seems rather unlikely. Certainly, a tendency toward immunological inhibition of fertilization could lead to selection effects. In view of the increased incidence of HL-A antibodies with increasing parity, such selection should increase in severity with parity, but no such effects have, so far, been observed³². The presence of HL-A antigens on sperm has been shown by the work of Fellous *et al.*⁷⁹ and Ceppellini *et al.*⁸⁰. To my knowledge, however, no data are available on the presence or absence of HL-A antibody in the cervical mucosa or secretions. Similar mechanisms could of course apply with respect to, for example, the ABO system, though the evidence for the presence of ABO antigens on sperm is still equivocal.

Function of Other Genes

So far this discussion of the possible factors maintaining the HL-A polymorphism has been limited to the significance of the serologically identifiable antigens controlled by the closely linked LA and 4 loci. As already mentioned, however, it is probable that there exist hundreds or even thousands of cistrons between these two loci. Selection acting on these many linked loci could easily be responsible for the maintenance of polymorphism at the LA and 4 loci. It is usually very difficult, if not impossible, to distinguish the selective effects of a given detectable gene locus from those that may be due to closely linked loci, the products of which are not readily detectable. Thus, the LA and 4 antigens may simply be acting as markers for the overall effects of the many other loci in that same chromosome region. Studies on the population genetics of linked loci, stimulated by Fisher's⁷⁸ original suggestion as to how certain types of selective interaction may favour close linkage, have shown that there are reasons for expecting that, at least in some cases, closely linked genes may be concerned with related or interdependent functions (for review and further references, see, for example, refs. 23 and 24). It seems natural, therefore, to speculate on the possible functions of the many genes in the HL-A region and their biological significance in relation to the maintenance of the HL-A polymorphism.

There are several indications for the existence of at least some other genes in the HL-A (or H2 regions) that may be involved in the synthesis or control of cell-surface structures. Suggestive evidence comes from the work of McDevitt *et al.*⁴⁹ on the immune response gene *Ir-1* in the mouse, which controls the level of antibody response to certain synthetic branched multi-chain polypeptide antigens. This gene has been shown by recombination studies to lie in the right half of the H2 region near the K end. McDevitt⁸¹ has made the stimulating and provocative suggestion that the *Ir-1* gene, and possibly others like it in the same region, controls the synthesis of non-immunoglobulin T-cell antigen receptors. It has so far been generally

assumed that both B and T cell antigen receptors might belong to one of the known classes of immunoglobulin, because the antigen binding specificity of such receptors must be comparable with that of immunoglobulins (see, for example, ref. 82). It seems, however, that at least in man and mouse, the immunoglobulin determining genes are not closely linked to the major histocompatibility region. The evidence for this comes from data in man and mouse based on allotype studies which show close linkage between the genes for H chain constant regions (see, for example, refs. 83 and 84), and data showing an absence of close linkage between H2 and the mouse allotypes⁸⁴ and between HL-A and the human allotypes⁸⁵. There is also evidence from studies on rabbit allotypes located in the variable region that, at least in this organism, constant and variable chain genes are relatively closely linked^{86,87}. If these results extrapolate to man and mouse, then close linkage between H2 or HL-A and any of the known immunoglobulin determining genes seems to be ruled out. In this case antigen receptors determined by genes in the H2 region could not belong to any of the known classes of immunoglobulins. McDevitt's hypothesis, therefore, suggests the existence of a new class of molecules controlled by genes in the H2 region which have, at least to some extent, properties comparable with immunoglobulins with respect to the ability to recognize specific antigens.

Further evidence for cell-surface structure controlling genes in the HL-A or H2 regions comes from studies on the mixed lymphocyte culture (MLC) reaction, which generally occurs when lymphocytes from different individuals are cultured together and stimulate each other to enlarge and then divide. It has been shown by Bach and Amos⁸⁸, and confirmed by Shellekens *et al.*⁸⁹ among others, that sibs who are identical at the HL-A locus do not stimulate each other in an MLC test, whereas almost all other combinations of individuals do, placing special emphasis on the control of the MLC reaction by the HL-A system. Subsequently, rare combinations of HL-A identical sibs have been found who do stimulate each other in an MLC test^{90,91}. This has been taken to indicate that there exists a locus closely linked to LA and 4, but separable from it by a recombination fraction of the order of 1%, which at least contributes to, if not determines by itself, the MLC response^{91,92}. Supporting evidence comes from the observation that HL-A identical unrelated individuals mostly, though not always, stimulate each other in MLC tests^{93,94}. Similar data to those on the MLC reactions have been obtained from studies on the relation between skin graft survival and HL-A incompatibility. Thus, it has been shown that HL-A identical sibs tolerate each other's skin grafts significantly longer than other pairwise combinations (see, for example, ref. 95) and that this effect of HL-A compatibility is much less in HL-A identical unrelated individuals⁹⁴. It seems possible, in fact, that graft rejection caused by differences in the HL-A region is determined wholly, or at least in part, by differences at loci in the HL-A region, other than the LA and 4 loci themselves. The serologically detectable histocompatibility antigens may merely be markers for differences at closely linked loci which are not themselves serologically detectable. Analogous data on the MLC test and skin graft survival have been obtained in relation to the H2 system in the mouse. These studies, by Demant, Ivanyi and their colleagues (ref. 96 and P. Demant, personal communication), have suggested that loci controlling MLC response and skin graft survival may be nearer the K than the D end of the H2 region. Preliminary observations suggest that the same may be true with respect to the 4 locus of the HL-A system, indicating that the 4 locus may be the homologue of the K end of the H2 region (refs. 97 and 98 and T. Oliver and H. Festenstein, personal communication).

Differentiation Antigens

It is generally accepted that cell to cell recognition by like or by associated cells may play a very important part in tissue differentiation and morphogenesis (see, for example, ref. 99).

This recognition is most likely to be mediated by cell surface structures which, in appropriate conditions, may perhaps be detected as cell surface antigens using serological techniques. Such antigens should be specific to a given type of cell, perhaps even at a given time during development, and so should behave as differentiated products. Antigens which seem to satisfy these criteria include the θ , Ly^a and Ly^b lymphocyte antigens of the mouse and have been called by Boyse and Old¹⁰⁰ "differentiation antigens". Interaction between cells of given type, whether alike or different, most probably requires two classes of molecules, as has been emphasized recently by Burnet¹⁰¹ and Jerne¹⁰² especially in relation to the immune system. One of these classes is the differentiation antigens. The other must be a class of molecules whose function is to recognize the differentiation antigens and so to mediate the interaction between appropriate types of cells during development. These molecules, which may be called "recognizers", must have properties which are analogous to those of the antibody molecules. A given type of cell should both have differentiation antigens and produce recognizers, which latter are not, however, necessarily directed at its own differentiation antigens. Thus, stable associations between two different types of cells could, perhaps, be maintained if each produced recognizers corresponding to the other's differentiation antigens.

I suggest the hypothesis that there is a large number of genes in the HL-A (or H2) region, other than those determining the serologically detectable histocompatibility antigens, which either control the synthesis of a particular class of differentiation antigens and/or control the synthesis of a class of recognizers. If the HL-A or H2 linked genes control differentiation antigens, it is already suggested from the work of Boyse and Old and others^{100,103} that by no means all differentiation antigens are controlled by genes that are linked to the major histocompatibility region. Those that are, however, could easily include the Ir, MLC and skin graft loci discussed here. It is worth noting in this context that there is some evidence which suggests that the ability to stimulate in the MLC test is specific to the lymphocyte¹⁰⁴. The function of the serologically detectable HL-A antigens, which seem to be present on nearly all tissues, might be analogous to that of the constant regions of the immunoglobulins, as has been suggested independently by Amos *et al.*^{85,91} and van Rood *et al.*⁹³ in somewhat different but nevertheless comparable contexts. The differentiation antigens controlled by genes in the HL-A region, might, for example, form functional units by combining with one or more of the peptides controlled by the LA and 4 loci. Such interactions could, perhaps, account for some of the reports of anomalous behaviour of HL-A antigens in differentiated tissues, such as their occasional absence from platelets when detected on lymphocytes¹⁰⁵, and their presence on kidney cells when not detected on lymphocytes^{106,107}. Anomalies involving the expression of HL-A antigens on tumour cells, for example, could perhaps also be explained in a similar way. Similar explanations could in addition account for the extensive occurrence of cross reactions (see, for example, refs. 92 and 108) among antigens of the HL-A system.

Differentiation Antigens and the Immune System

A much discussed and provocative hypothesis for the somatic generation of antibody diversity which functionally interrelates immunoglobulins and histocompatibility antigens has recently been put forward by Jerne¹⁰². He has suggested that there is a germ line set of ν genes (which code for the variable regions of antibody molecules) that determine the combining sites of antibodies directed at all the histocompatibility antigens of the relevant species. In any individual, these immunoglobulin ν genes are divided into two sets. The first set, S , corresponds to those for the histocompatibility antigens which the individual possesses, and the second, A , corresponds to those directed against all the other histocompatibility antigens of the species

which the individual does not possess. It is the set S which, in connexion with the development of tolerance, is presumed to give rise, by random somatic mutation followed by selection, to the diverse somatic complement of antibody molecules. Tolerance for histocompatibility antigens is achieved because cells expressing non-mutant set S ν genes are eliminated by the antibody they produce which is directed against their own antigens. A principal, almost insurmountable, difficulty with Jerne's hypothesis as it stands is that it seems to require strict parallel evolution at the population level of histocompatibility antigen genes and immunoglobulin ν genes. Thus, apparently, as soon as a new histocompatibility antigen arises by mutation or recombination, the corresponding germ line ν gene coding for the antibody specificity directed against this new antigen must somehow almost immediately spread through the whole species. It is almost impossible to conceive of a selective mechanism which could be powerful enough to effect such a comparatively rapid change, especially in view of the fact that the two sets of genes are not linked. The parallel evolution of antigen and immunoglobulin genes still seems to remain a problem even if the strict assumption made by Jerne that an individual must have ν genes for all the histocompatibility (H) antigens of the species is relaxed. A minimum requirement of the theory is that an individual carries enough ν genes directed against the various H antigens to make it very likely that at least one or more of these correspond to his own H antigens; in other words, that his set S is not empty. Otherwise the individual will be unable to develop a generalized immune response and so will, presumably, be at a severe selective disadvantage. An individual's fitness may, in fact, increase as the number of ν genes in the set S increases up to its maximum, as this may extend the range of his immune response. Consider, now, the situation of an individual carrying a comparatively new histocompatibility antigen before there has been time for a corresponding new ν gene to spread through the population. The probability that his set S is empty will be increased, or more generally the average number of ν genes in his set S will be decreased, because there is at least one of his H antigens with respect to which no corresponding ν gene exists in the population. This will, presumably, lead to a selective disadvantage for individuals carrying a new histocompatibility antigen. This is in direct contradiction with the suggestion, discussed earlier on, that there may be a consistent selective advantage for genes determining new histocompatibility antigens. I should like to suggest a modification of Jerne's hypothesis which overcomes this difficulty and which is in line with the ideas discussed above on the relation of histocompatibility antigens to the genetic control of differentiation antigens and their recognizers. The suggestion is that the set S of ν genes is directed not at the histocompatibility antigens themselves but at the differentiation antigens, which are common to all individuals of the species and of which many, as suggested above, may be genetically and functionally connected with the serologically detectable histocompatibility antigens.

There is then no strict need for the complete complementary A set of ν genes, or for the problematical concomitant evolution of histocompatibility antigen genes and immunoglobulin ν genes. The existence of some ν genes directed at histocompatibility antigens (or their cross-reactive subcomponents) could, however, still be invoked to explain phenomena such as allo-aggression which are discussed by Jerne in relation to his theory. If, as Jerne suggests, the immune system has evolved from the machinery for cell to cell recognition in multicellular differentiated organisms, then the set S of immunoglobulin ν genes may have evolved from the set of genes controlling the recognizers of differentiation antigens. This set of genes, some of which, as suggested above, may be in the major histocompatibility region, may have been duplicated and transposed during evolution in such a way as to allow the evolution of the immune system to proceed without disturbing the control of multicellular development and differentiation. Multicellular differentiation does, of course, occur in organisms

which have no obvious immune system. The evolution of an immune system from duplication of the recognizers is likely to have led to a relaxation of the strict correspondence between ν genes and differentiation antigens. Thus, not all differentiation antigens would necessarily have a corresponding ν gene, nor would all ν genes have a concomitant differentiation antigen. Though there might still remain some mutual restrictions on effective mutations to new ν genes and differentiation antigens, these two sets of genes may have been largely "uncoupled" during the evolution of the immune system. The recognizers needed for multicellular development and differentiation must, of course, remain strictly coupled to the differentiation antigens.

There is a possible analogy between the recognizers and the blocking factors invoked by the Hellströms and their colleagues¹⁰⁹⁻¹¹¹ to explain some aspects of immune tolerance, the factors shown by Ceppellini and colleagues^{92,112} to inhibit the MLC reaction and the Ir-I gene T antigen receptors postulated by McDevitt.

The challenge presented by this hypothesis is to identify the differentiation antigens and their recognizers and to see which, if any, of the corresponding genes are linked to the HL-A or H2, or other histocompatibility regions. In our laboratory we have initiated studies along these lines, making use of the techniques of somatic cell genetics, using cell hybridization.

The clear implications of this discussion for the maintenance of the HL-A polymorphism are that selective forces connected with mutations affecting the genes for the differentiation antigens and their recognizers may play a major role in the evolution of the HL-A polymorphism. Histocompatibility polymorphism, like the immune system, may have been an evolutionary byproduct of the need to develop a cell-cell recognition system for the differentiation and morphogenesis of multicellular organisms.

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X-ray Diffraction Study of Binding of 2,3-Diphosphoglycerate to Human Deoxyhaemoglobin

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DPG has a two-fold effect on human deoxyhaemoglobin. It both stabilizes and slightly distorts the S form, and may therefore affect the solubility.

HAEMOGLOBIN and D-2,3-diphosphoglycerate (DPG) are the principal organic constituents inside the human erythrocyte. Both molecules have an *in vivo* concentration of 5 mM, but the function of DPG was unknown until the discovery^{1,2} that it lowers the oxygen affinity of haemoglobin and thus facilitates the unloading of oxygen. Subsequent research has shown that DPG regulates oxygen transport by binding preferentially to deoxyhaemoglobin in the ratio of 1 mol DPG/mol haemoglobin tetramer, without diminishing the cooperative nature of ligand binding³.

Several biochemical studies concern the DPG binding site⁴⁻⁷, in particular the work of Bunn and Briehl on a variety of human haemoglobins implicating histidine H21(143) β and the N-terminal amino-group of the β -chain⁵. When Perutz examined this region on an atomic model of horse deoxyhaemoglobin, he found that a molecule of DPG could be accommodated well in the opening of the central cavity with valine NA(1), lysine EF6(82), and histidine H21(143) of both β -chains complementing the negative charges of DPG⁸. In oxyhaemoglobin, on the other hand, this complementary stereochemistry with DPG was lost. I undertook this X-ray study to observe directly the interaction of DPG with deoxyhaemoglobin.

Table 1 Unit Cell Parameters of Native Deoxyhaemoglobin A Crystals and of Crystals soaked in 70% MPD+1 mM DPG

	<i>a</i>	<i>b</i>	<i>c</i>	β
Native haemoglobin A	63.1	83.5	53.8	99.18°
DPG/MPD soak	63.1	83.9	54.1	99.18°

Muirhead and Greer have solved the structure of human deoxyhaemoglobin to a resolution of 3.5 Å⁹, using crystals grown from concentrated ammonium sulphate solutions buffered with ammonium phosphate to pH 6.5¹⁰. The mother liquor for these crystals is, however, unsuitable for the study of DPG binding, as even moderate salt concentrations dissociate the DPG-deoxyhaemoglobin complex¹¹. To circumvent this problem, crystals grown in these high-salt conditions were dried superficially with filter paper, and then placed directly into solutions composed of seven volumes 2-methyl-2,4-pentanediol (MPD) and three volumes deionized water. Other crystals were soaked in identical solutions of 70% MPD except that three volumes of 3.3 mmol DPG (pH 6.9) replaced the water. Crystals soaked in these solutions for five days lost almost all diffracting power, but crystals mounted in quartz

capillaries after a one-day soak retained three-dimensional order, and showed only minor changes in unit cell dimensions (Table 1). Also, as precession photographs revealed large intensity changes in only the very low order reflexions, one day appears to suffice for substantial diffusion of the MPD solution into (and electrolytes out of) the interstices between protein molecules¹². To keep the crystalline haemoglobin reduced, all these manipulations were carried out in a nitrogen-filled glove box, and the MPD was degassed immediately before use.

Diffraction data were collected to a resolution of 3.5 Å on a Hilger-Watts four-circle diffractometer. Difference electron density maps were then calculated using the known phases of deoxyhaemoglobin A⁹ and the following structure amplitudes:

$$\text{Map 1} = |F|_{\text{Hb (70\% MPD)}} - |F|_{\text{Hb (native)}}$$

$$\text{Map 2} = |F|_{\text{Hb (70\% MPD + 1 mM DPG)}} - |F|_{\text{Hb (native)}}$$

$$\text{Map 3} = |F|_{\text{Hb (70\% MPD + 1 mM DPG)}} - |F|_{\text{Hb (70\% MPD)}}$$

where the subscripts refer to the native high-salt crystals and to crystals soaked in 70% MPD and 70% MPD+1 mM DPG. Any structural perturbations arising solely from the change in mother liquor should be observed in Map 1. The main property of this difference map is a high background, which is probably caused by small shifts of the haemoglobin molecules relative to each other accompanying the small lattice changes. Protruding above this background, midway up the central cavity, are two pairs of positive peaks related by the molecular dyad. These peaks (the only significant features on the map) have been tentatively interpreted as counterions associated with arginine G6(104) β and glutamate G3(101) β . These counterions may be either absent or more diffuse in concentrated ammonium sulphate, but in the MPD medium of higher dielectric constant they take up fixed positions detectable on an electron density map.

Map 2 corroborates the "solvent effects" detected in Map 1, but shows only vague evidence of DPG binding. The DPG binding site is clearly revealed, however, in Map 3 (Fig. 1b) where the high non-random background—common to the first two maps—has been subtracted. The difference electron density of Map 3 appears to possess (at least to a resolution of 3.5 Å) the same non-crystallographic dyad axis as the electron density map of the native protein⁹, indicating that the asymmetric DPG molecule is binding to the haemoglobin tetramer in two different orientations related by a 180 degree rotation, that is the difference map represents the binding of a "symmetry averaged" DPG molecule consisting of two phosphate groups and two (half-weight) carboxyl groups. By averaging the electron density at equivalent points related by the symmetry axis, this disordering has been exploited to enhance the genuine features and reduce the random background of Map 3.

The only binding site found in this study is shown in Fig. 1a and b, and, as predicted^{5,8}, the DPG plugs the entrance of the central cavity between the N-terminal amino-groups of the β -chains. The pair of positive and negative peaks labelled P1 and p1 show that these α -amino-groups move towards, and interact with, the DPG anion, and peaks P2 and p2 show a

similar movement and interaction for the imidazole groups of histidines H21(143) of β_1 and β_2 . A similar pair of peaks (not shown) indicate that the β_1 and β_2 histidines NA2(2) are also binding. Lysines EF6(82) β_1 , β_2 are the only other basic groups close enough to interact with DPG. There is, however, only a small amount of electron density to indicate their positions in the native map and, although the negative peak $p3$ implies a movement of the side chain, no corresponding positive peak can be found. Perhaps the huge negative peak $p4$ obscures a positive one that would indicate interaction of the lysines with the DPG carboxyl group. This hypothetical positive peak should, in any case, be small since the "symmetry averaged" DPG molecule contains only half a carboxyl group for each lysine.

The peak labelled X^- on the native electron density map (Fig. 1a) is replaced by the massive negative peak $p4$ in the difference map. Originally, X^- was interpreted as the side chain of asparagine EF4(80) β , but close comparison of the electron density map with the EF corner on an atomic model of horse deoxyhaemoglobin shows that the peak cannot be part of the β -chain at all. The size of $p4$, the absence of any cor-

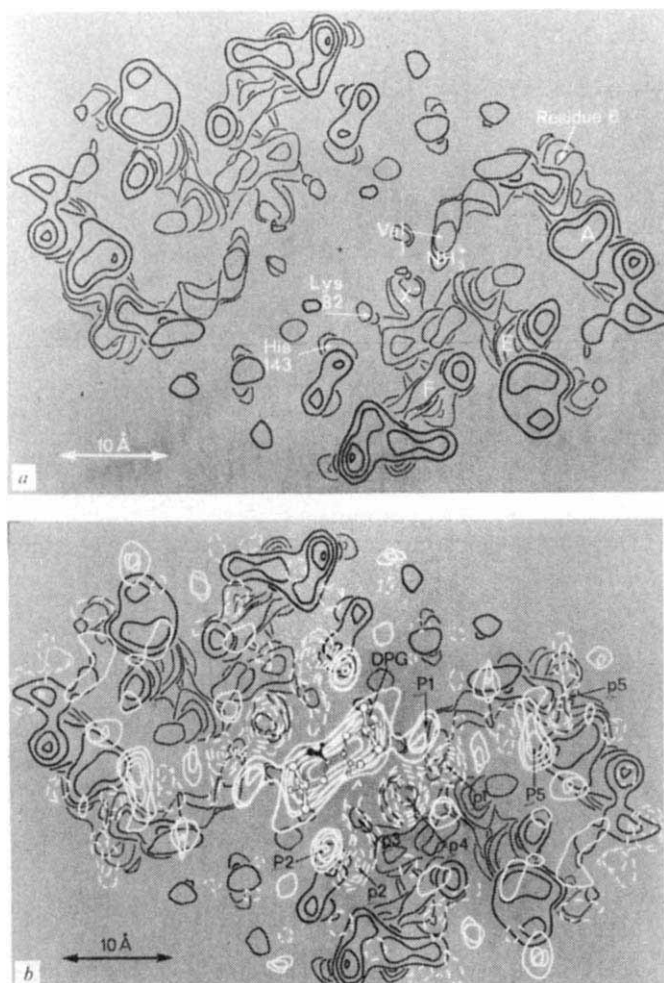


Fig. 1 Fourier maps showing the DPG binding site at the entrance to the central cavity between the N-terminal amino-groups of the β -chains. *a*, Native human deoxyhaemoglobin electron density map at 3.5 Å resolution (sections -15 to -23 Å). This region includes helices A, E, and F and residues Val 1, Glu 6 (the site of the sickle cell mutation), Lys 82 and His 143 of the β -chain. The peak marked X^- has been identified as an inorganic anion (see text). *b*, Sections -18 and -19 of the DPG difference map (white contours) are superimposed on the native protein electron density (black contours). Positive difference electron density is marked by solid white contours and upper-case letters. Negative difference electron density is marked by dashed white contours and lower-case letters. A "symmetry averaged" DPG molecule (see text) has been superimposed to fit the large positive difference peak on the dyad axis.

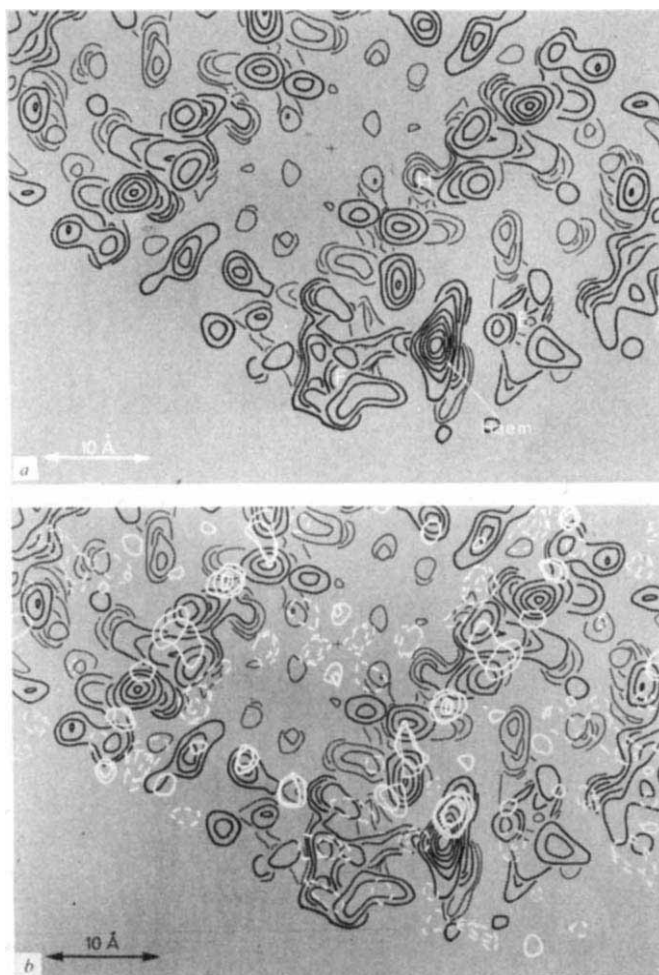


Fig. 2 Fourier maps showing the perturbation of the β haem environment on binding DPG. *a*, Native human deoxyhaemoglobin electron density map at 3.5 Å resolution (sections -8 to -14 Å). The helices E, F, and H are labelled along with the β haem group. *b*, Sections -8 and -9 of the DPG difference map (white contours) are superimposed on the native protein electron density (black contours). The meaning of the contours is as in Fig. 1.

responding positive peak on the difference map, and the fact that the EF corner is relatively unperturbed, also suggest a different interpretation. Mrs J. M. Baldwin suggested to me that X^- is in fact an inorganic anion, probably sulphate or phosphate, and that the negative peak $p4$ simply represents the displacement of this anion by DPG. In the absence of DPG, this anion fits snugly into a small pocket, binding ionically to N-terminal amino-group of the β -chain and lysine EF6(82) β , and may hydrogen bond to a main chain NH group. The evidence for the interaction of lysine 82 comes mainly from the position of the negative peak $p3$ on the difference map.

The most conspicuous effect of DPG on the structure of each β subunit is a movement of the A-helix. This is indicated by a series of negative difference peaks on the outer surface of the helix and a corresponding set of positive difference peaks on its inner surface. This structural perturbation arises because in the absence of DPG the NH_3^+ groups of valines 1 β and the histidines 2 β are a little (probably about 2 Å) too far apart to form salt bridges with the phosphates of a fully extended DPG molecule. When DPG attracts these groups, the A-helices are pulled along and move closer towards helix E and the EF corner. Another perturbation to the β chain, shown in Fig. 2a and b, manifests itself in a row of positive and negative peaks flanking helix H, indicative of a movement of this helix away from the central cavity and towards the haem group. The meaning of this feature is not yet clear, for, taken at face value, it would imply a movement of helix H towards the

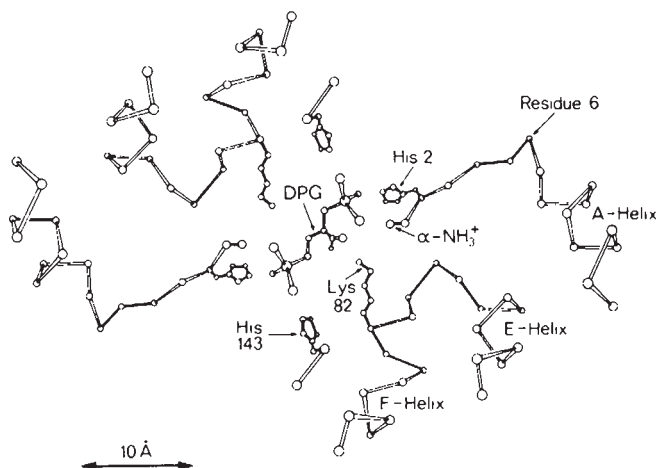


Fig. 3 Sketch showing the binding of DPG to human deoxyhaemoglobin. The stereochemistry of DPG complements the basic residues of the central cavity to form salt bridges with valines 1 and histidines 2 and 143 of both β -chains, and with lysine 82 of one β -chain. This binding pulls the A-helix and the haemoglobin S mutation site (residue 6) towards the E-helix and the EF corner.

haem group by about 1 Å, involving a compression of the entire β -subunit, but as it is already closely packed this seems unlikely. Another possible explanation would be that the entire β subunit has moved outwards, away from the central cavity, but the evidence relating to these two alternative interpretations is still ambiguous.

This X-ray study confirms that one molecule of DPG binds to one molecule of deoxyhaemoglobin, and that it takes up a stereochemically complementary position on the two-fold symmetry axis, plugging the entrance to the central cavity. Its anionic groups form salt bridges with seven cationic groups of the β -chains which include the valines 1, histidines 2 and 143, and one of the lysines 82 (Fig. 3). This complementary stereochemistry is specific for the quaternary deoxy structure and is lost on transition to the oxy form. Thus DPG stabilizes the former at the expense of the latter, thereby shifting the allosteric equilibrium towards the form with the lower oxygen affinity. In terms of the allosteric theory of Monod *et al.*¹³, this would be expressed by an increase in the value of the allosteric constant L .

The difference map, however, shows that it does more than that. By pulling the A-helices of the two β -subunits close together and pushing the H-helices (or the entire β -subunits) further apart, DPG actually induces subtle changes in the tertiary (and possibly in the quaternary) deoxy structure of the β -subunits. The exact magnitudes of these movements are still unclear, but may be of the order of 1–2 Å. If they oppose the transition of the tertiary structure from the deoxy to the oxy form, then DPG should directly decrease the oxygen affinity of the β -chains. In terms of allosteric theory¹³, it should increase the value of the constant c .

There are several other interesting points of detail. The binding of histidines 2 β in human haemoglobin explains the relatively smaller effect of DPG on the oxygen affinity of horse haemoglobin, in which residue 2 β is a glutamine¹⁴. Similarly, the binding of histidines 143 β explains the large effect of DPG on adult, as compared with foetal, human haemoglobin, in which residue 143 β is a serine^{5,8}. A huge negative peak on the DPG difference map (peak p4 in Fig. 1b) reveals the binding site for an inorganic anion (peak X⁻ in Fig. 1a) and gives a structural explanation for the competitive nature of DPG and inorganic salt binding¹¹. Also, horse and human haemoglobin have similar amino-acid sequences at the entrance to the central cavity, but the electron density map of horse oxyhaemoglobin shows no evidence of salt binding at this site. The electron density map of its deoxy form, on the other hand (crystallized from 2.5 M phosphate buffer), does show peaks in the exact

positions of the phosphate groups of DPG now found in the human form, clearly representing inorganic phosphate ions. These observations suggest that phosphate and possibly other anions may be needed to stabilize the quaternary deoxy—but not the oxy—structure, so that in their absence the allosteric equilibrium would be shifted towards the oxy structure. This would explain the increased oxygen affinity observed in haemoglobin solutions of very low ionic strength¹¹.

The interaction of the anionic groups of DPG with the cationic ones of the β -chains must affect the pK s of both sets of groups in opposite directions. Experimental evidence shows that the Bohr effect in human haemoglobin is increased by as much as 50% in the presence of DPG^{6,15}, which means that the increase in pK s of the six cationic groups (four histidines and two α -amino-groups) dominates over the decrease in pK of the second ionization of the two phosphates. Clearly, any explanation in terms of only the α -amino-groups would appear to be oversimplified¹⁶.

The foregoing results also have interesting implications for the mechanism of sickling and its inhibition by cyanate¹⁷. Murayama *et al.*¹⁸ have postulated that “the haemoglobin S molecule can undergo a conformational change such that the amino terminal valyl can interlock with the genetically induced valyl residue at position 6. This allows cyclization of the peptide chain from the first carbonyl to the NH of the fourth threonyl by hydrogen bonding. . . . We have a notion that the cyclization appears to be a necessary and sufficient condition for the molecules to stack”. This postulated cyclization should be inhibited by DPG which locks the valines 1 in the internal cavity and leaves the side chain of residue 6 (glutamate or valine) exposed on the surface of helix A. In fact, DPG enhances the gelling of haemoglobin S¹⁹ which indicates that this theory is incorrect.

Reaction with cyanate blocks the interaction between DPG and the α -amino-groups of valine 1 β by forming $—NHCONH_2$ groups in their place²⁰. Hence the inhibitory effect which cyanate has on the sickling process¹⁷ is likely to be due to a reduction of the affinity of deoxyhaemoglobin S for DPG, and a consequent shifting of the allosteric equilibrium towards the oxy form²¹.

DPG has a two-fold effect: it stabilizes the deoxyhaemoglobin structure, but it also alters it slightly, so that the distance between valines 6 β_1 and 6 β_2 in deoxyhaemoglobin S is about 2 Å shorter in the presence of DPG than in its absence. This contraction may affect the solubility of deoxyhaemoglobin S, but it is not possible to predict whether it will increase or decrease it. It should, however, be possible to measure this by studying the effect of DPG on the gelling of deoxyhaemoglobin S under oxygen-free conditions, that is, under conditions where DPG would not significantly increase the concentration of the quaternary deoxy structure.

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Direct Recording of Oxyhaemoglobin Dissociation Curve *in vivo*

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An experimental technique for *in vivo* measurements of O₂ dissociation curves is described. This allows rapid determination of P_{O₂} and S_{O₂}.

THE oxyhaemoglobin dissociation curve (O₂ dissociation curve), representing the relation between oxygen tension (P_{O₂}) and oxygen saturation (S_{O₂}), ranks high among the data essential for the study of blood gas transport. Although the influence in mammalian whole blood of pH, P_{CO₂}, and temperature on the shape and position of the O₂ dissociation curve was well known, the curve as such was until recently considered to be rather constant for a given species and certainly not subject to rapid variations within the same individual. The discovery that organic phosphates, especially 2,3-diphosphoglycerate (DPG), act as a cofactor in the oxygenation-deoxygenation reaction and consequently have a strong influence on the O₂ affinity of haemoglobin¹⁻³ has shed new light on this matter. As DPG is an intermediate in anaerobic glycolysis—the main energy releasing metabolic pathway in the red blood cell—its concentration can change rapidly, resulting in a significant shift of the O₂ dissociation curve within a few hours or less. For the study of these effects, a rapid and easily repeatable method for the determination of the O₂ dissociation curve would be a valuable asset.

Until recently, O₂ dissociation curves have been determined by equilibrating a series of blood samples with gas mixtures of different P_{O₂}. After determining P_{O₂} and S_{O₂} of the equilibrated samples the corresponding values of the two variables were plotted as points on rectangular coordinate paper, and the best fitting curve drawn through these points. For equilibration various tonometers^{4,5} were used. The development of reliable membrane-covered Pt electrode catheters for the intravascular determination of P_{O₂} (ref. 6) and the construction of a dependable fibre optic oximeter⁷ has brought the simultaneous recording of intravascular P_{O₂} and S_{O₂} within the realm of possibility. It took only one further step to feed the output signals of the two measuring systems into an x-y recorder for the direct recording of the O₂ dissociation curve *in vivo*.

The intravascular P_{O₂} measurement is based on the polarographic principle and is carried out using a Clark type catheter-mounted electrode. The tip of the catheter consists of a silver

housing which serves as reference electrode and contains a ring-shaped Pt electrode covered with a 6 µm 'Teflon' membrane⁶. With this electrode flow artefacts have proved to be less than 1% of the output signal when the flow velocity past the electrode is above 5 cm s⁻¹. The 95% response time is less than 0.5 s. After intravascular conditioning of the electrode, the drift of the output signal is negligible. The P_{O₂} measuring system is calibrated *in vivo in situ*. To this end the experimental animal is ventilated with gas mixtures of different P_{O₂} and each time a steady state is reached, a blood sample is withdrawn for the determination of P_{O₂} using a conventional method (Radiometer P_{O₂} electrode, type E 5047).

The intravascular S_{O₂} measurement is carried out using a fibre optic catheter (American Optical Company). This catheter contains two light-conducting fibre bundles, one for the incident light, the other to conduct the light reflected by the erythrocytes to the measuring system. The reflected light is measured in two wavebands (λ_{max} = 640 and 920 nm) using a dichroic mirror and two filter-photocell combinations⁸. The measurement around λ = 640 nm is sensitive for changes in S_{O₂}, the other measurement serves to compensate for the effect of other factors influencing light reflexion, especially changes in blood flow velocity past the catheter tip. The ratio of the two photocell output signals (R⁶⁴⁰/R⁹²⁰) is recorded. The relationship between log (R⁶⁴⁰/R⁹²⁰) and S_{O₂} proved to be almost linear. Remaining flow artefacts are effectively suppressed by appropriate electronic filtering^{9,10}. The S_{O₂} measuring system is also calibrated *in vivo in situ*, using a conventional transmission oximeter (Radiometer, type OSM 1) for the measurement of S_{O₂} of blood samples.

O₂ dissociation curves have been recorded *in vivo* using mongrel dogs (12–30 kg) in thialbarbitone ('Kemithal'; 35 mg kg⁻¹) anaesthesia after premedication with acepromazine maleate ('Ventranquil'; 0.5 mg kg⁻¹ intramuscularly). Spontaneous ventilation was suppressed with pancuronium bromide ('Pavulon'; 0.1 mg kg⁻¹) and intermittent positive pressure breathing maintained using a volume-controlled respirator and a semi-closed circuit fed with various mixtures of O₂ and N₂. Body temperature was kept within 37°–39° C with the aid of an electric blanket. After intravenous injection of 3 mg kg⁻¹ heparin, a sampling catheter was introduced into a peripheral artery for the determination of pH, P_{CO₂}, plasma bicarbonate and haemoglobin concentration and for calibration of the P_{O₂} and S_{O₂} measuring systems. The electrode catheter and the fibre optic catheter were introduced into the abdominal aorta by way of the femoral arteries. Under X-ray control the catheter tips were placed in position close together.

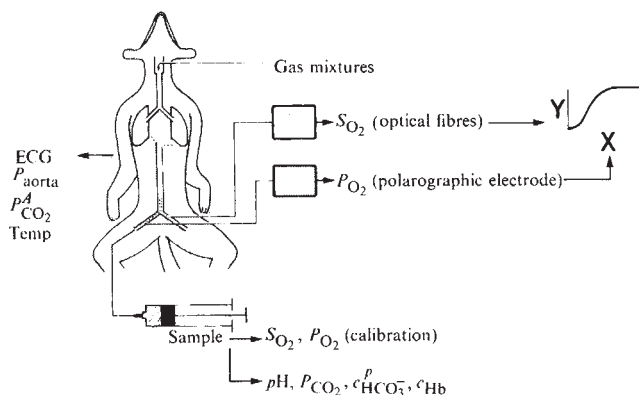


Fig. 1 Schematic diagram of experimental set-up for direct recording of O_2 dissociation curves *in vivo*. The arterial O_2 saturation (S_{O_2}) is measured using a catheter containing optical fibres. The arterial O_2 tension (P_{O_2}) is measured using a polarographic electrode catheter. The catheter tips are situated in the abdominal aorta. The dog is on intermittent positive pressure breathing using various N_2/O_2 mixtures. In addition to P_{O_2} and S_{O_2} , electrocardiogram (ECG), arterial blood pressure (P_{aorta}), end-expiratory CO_2 tension ($P_{CO_2}^A$), body temperature (Temp), arterial pH (pH), arterial CO_2 tension (P_{CO_2}), plasma bicarbonate concentration ($c_{HCO_3^-}$) and haemoglobin concentration (c_{Hb}) are measured.

The response times of the two measuring systems were made equal by the use of appropriate electronic filters. The 95% response time of both systems is less than 0.5 s, thus allowing for fast changes to be truly recorded. The condition of the dog was monitored by recording an electrocardiogram, arterial blood pressure, end-expiratory P_{CO_2} and body temperature. All signals were fed into a multi-channel direct writing instrument (Elema EM 81). The S_{O_2} signal after linearization by means of logarithmic amplification and the P_{O_2} signal were also fed into an x - y recorder (Hewlett-Packard 7004 B). A schematic diagram of the experimental set-up is shown in Fig. 1.

For the actual recording of an O_2 dissociation curve, N_2 was substituted for O_2 in the gas mixture supplied to the breathing system, causing arterial P_{O_2} and consequently S_{O_2} to fall rapidly. When the electrocardiogram signalled the occurrence of myocardial hypoxia, the O_2 supply valve was fully opened and N_2 excluded; this resulted in a rapid rise of P_{O_2} and S_{O_2} . An arterial P_{O_2} near 10 mm Hg could be reached, after which good recovery could still be achieved provided the dog had been ventilated with 90–100% O_2 during at least

10 min before the hypoxic period. The whole procedure proved to take not more than 80 s (Fig. 2).

Fig. 3 shows two direct recordings of the O_2 dissociation curve. The ascending pathway does not coincide with the descending one, but displays a considerable displacement to the left. This is caused by the decrease in P_{CO_2} resulting from the high gas flow rate in the breathing system when the O_2 supply valve is fully opened (Bohr effect). Fig. 3 shows that the reproducibility of the method is excellent. To obtain more easily interpretable O_2 dissociation curves, however, a significant shift in P_{CO_2} and pH during the hypoxic period should be prevented. Therefore, in future experiments, the P_{CO_2} in the gas mixture supplied to the breathing system, rather the end-expiratory P_{CO_2} , should be kept constant. Moreover, arterial pH and P_{CO_2} should be checked regularly, by frequent sampling or, in the case of pH , by continuous recording using a suitable flow-through cuvette or pH catheter.

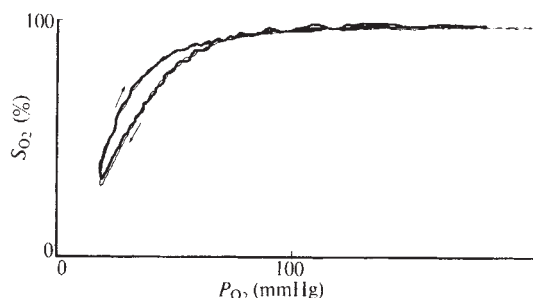


Fig. 3 O_2 dissociation curves recorded *in vivo* using an x - y recorder. The thin and the thick line represent two different experiments about 10 min apart. Displacement to the left of the ascending pathway resulting from a fall in P_{CO_2} (Bohr effect).

Recently a method has been described for the continuous recording of O_2 dissociation curves *in vitro*¹¹. As oxygenation and deoxygenation proceed very slowly in the set-up used for this purpose, recording of a single O_2 dissociation curve takes more than 100 min. This period is sufficiently long for appreciable metabolic changes to take place in the red blood cells. The O_2 affinity of haemoglobin could well change, especially by changes in the concentration of organic phosphates³, resulting in a more or less severe distortion of the recorded O_2 dissociation curve. The crucial advantage of the *in vivo* method is the rapidity with which an O_2 dissociation curve can be obtained, thus presenting an almost instantaneous representation of the relationship between P_{O_2} and S_{O_2} . If P_{CO_2} and pH can be sufficiently controlled during the recording of the O_2 dissociation curve *in vivo*, this method might become the method of choice for many investigations concerning the O_2 affinity of haemoglobin and its regulation by cofactors and environmental conditions.

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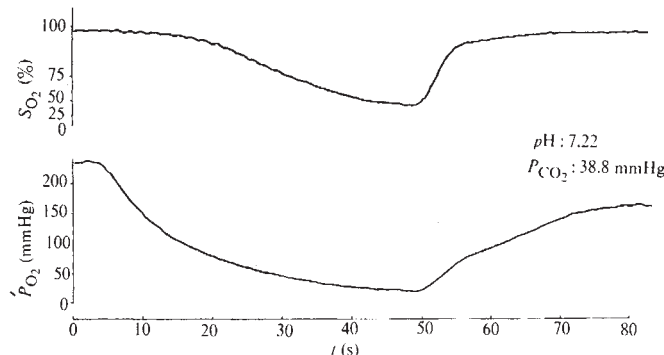


Fig. 2 Simultaneous recording of R^{640}/R^{920} as a measure of the arterial O_2 saturation (S_{O_2}) and arterial O_2 tension (P_{O_2}) during a short period of N_2 breathing followed by the administration of 100% O_2 . pH and P_{CO_2} measured immediately before N_2 breathing.

Segregation of Impurity Atoms in Niobium Oxide

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Low level impurities in niobium oxides are segregated and allow a regular modification of the parent structure around them. Models for two such doped oxides are presented.

HIGH resolution electron microscopy gives information about local order in crystals, of a kind unobtainable by other techniques. During work on the niobium oxides we have, by this method, obtained direct evidence that impurity or dopant atoms may be segregated in the form of extended defects.

Niobium oxides are structurally derived from the ReO_3 type, in a manner that enables very subtle changes in stoichiometry to be accommodated while retaining a high degree of local order. The structural principle¹ is that they are built up from rectangular columns or blocks of ReO_3 structure, with $[\text{NbO}_6]$ coordination octahedra linked through their vertices; the columns are $(m \times n)$ octahedra in cross section and infinite along the b axis of the crystal. There are two sets of such columns, with their cations at the levels $y=0$, $y=\frac{1}{2}$; these are spliced together across their faces, by edge sharing between their respective octahedra, to achieve the requisite anion/cation site ratio. Structures for two compounds of this type—the H and N modifications of Nb_2O_5 ($\text{Nb}_{28}\text{O}_{70}$ and $\text{Nb}_{16}\text{O}_{40}$ respectively), are shown in Fig. 1. Great flexibility in the anion/cation site ratio—and hence a complex

chemistry—is provided by possible variations in the cross sections of the sets of columns and the way that they are interfaced. In these structures, defects are not primarily point defects but are accommodated as extended defects, through the possibility of coherently intergrowing columns of the wrong cross section.

Since such defects imply, in many cases, a change in the anion/cation site ratio, they necessarily reflect the presence of ions in an anomalous valence state, implying fluctuations in composition within the crystal, arising from nonstoichiometry or from minor constituents such as impurities. The dimensions of individual columns are multiples of the octahedron diagonal of $\sim 4 \text{ \AA}$; a typical example is $12 \times 8 \text{ \AA}$ for a (4×3) column, as measured over the cation positions. If individual columns can be measured, their size $(m \times n)$ can be recognized; the anion/cation site ratio is thereby determined and their composition can be deduced. Fluctuations of composition at the unit cell level can thus be revealed.

This procedure is possible, using direct lattice imaging methods, for which the niobium oxides are well suited²⁻⁵. Although n -beam lattice fringe images of thick crystals present difficult problems of computation⁶, recent work has shown that thin crystal fragments ($< 100 \text{ \AA}$) approximate to amplitude objects. The enhanced scattering density at the interfaces results in a fairly clear delineation of the individual columns in a b axis projection (ref. 7 and Cowley and Iijima, unpublished results). To image their internal structure demands the highest point to point resolution rather than pure fringe resolution, and is just out of reach, with standard current instruments fitted with a goniometer stage (our work has been carried out on a 'JEM-100U' microscope). Cowley and Iijima, using a

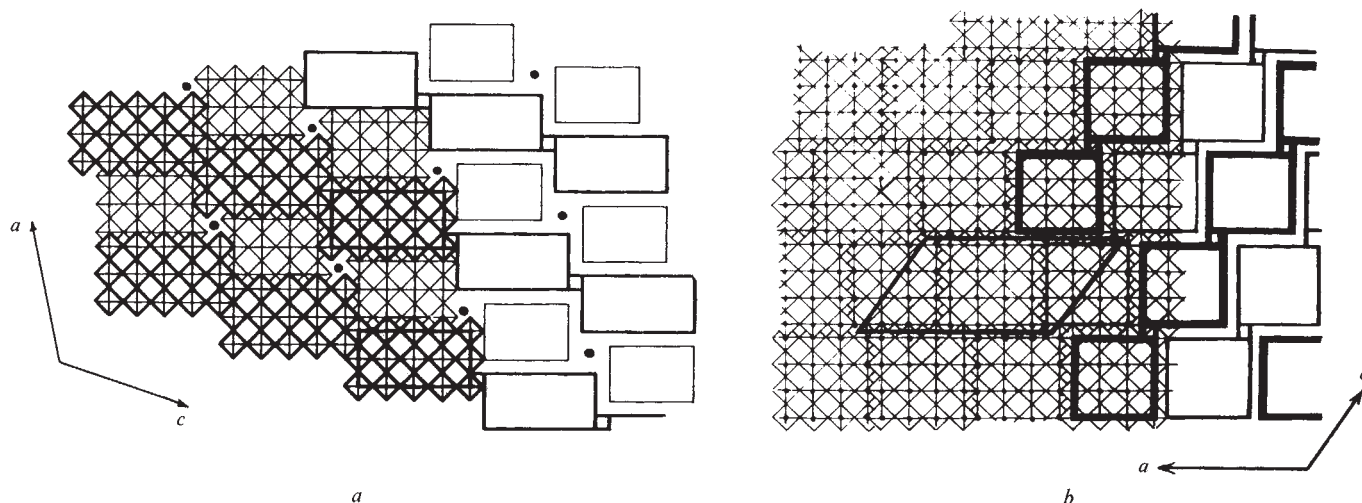


Fig. 1 *a*, Structure of $\text{H-Nb}_2\text{O}_5$ [010] projection, showing columns of octahedra, (5×3) in section, at one level (heavy outlines) and (4×3) columns at the second level. On the right hand side, a schematic representation outlines the rectangular columns as defined by the niobium atom positions. *b*, Structure of $\text{N-Nb}_2\text{O}_5$. Similar [010] projections showing the columns of (4×4) octahedra at both levels.

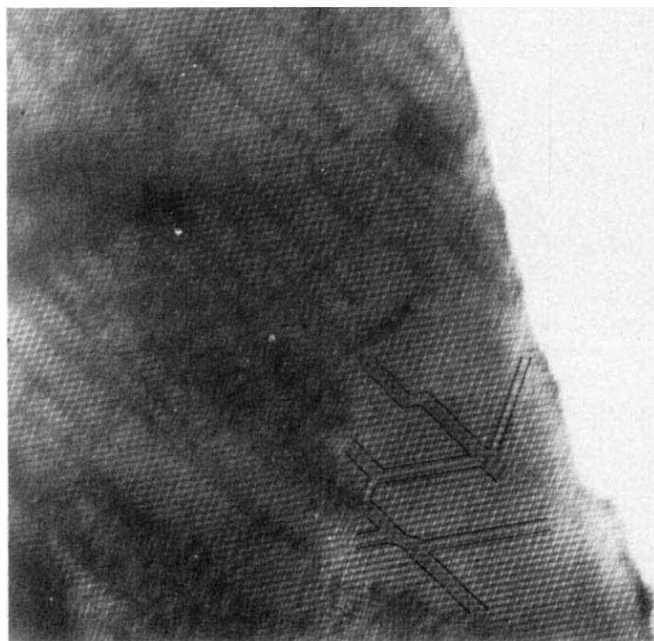


Fig. 2 Lattice image of $\text{H-Nb}_2\text{O}_5$, showing domain walls made up of arrays of wrong-sized columns.

modified 'JEM-100B', have, however, resolved the coordination octahedra in similar crystals; their micrographs confirm our interpretation of the image contrast. The position of contrast features—for example, maximum density at column interfaces—can be measured on the micrographs to about $2 \text{ \AA}$, so that the dimensions of anomalous columns can be assigned with some confidence. Structures in faulted regions can be built up in this way, consistent with the basic crystal chemical principles underlying all these structures.

Extended defects, with columns of anomalous size, are frequently observed. Some—twinned lamellae, insertions of structure belonging to a polymorph—involve no local change of composition. In others, the composition must differ locally from that of the matrix. In particular, we have recently observed that crystals may have extensive regions of perfect

structure, bounded by a network of domain walls of anomalous composition, one column in width, coherently intergrown with the perfect matrix on both sides. The chemistry of the system may be unambiguous. For example, Nb_2O_5 annealed in air has all the niobium in the $5+$ valence state. Deviations from stoichiometry, indicated by the column sizes that are found, can then arise only through the incorporation of foreign ions, of different valence. Thus, substitution of Cl^- or F^- for O^{2-} on anion sites increases the anion/cation ratio; replacement of Nb^{5+} by cations of lower valence lowers it. From the formation of regions with the wrong stoichiometry, we infer that foreign ions, at the impurity level, are not uniformly dispersed in solid solution, together with compensating point defects. They are segregated in such a way as to permit the structure to be modified around the sites at which they are incorporated. We illustrate this by two examples.

$\text{H-Nb}_2\text{O}_5$

Some of the metastable modifications of Nb_2O_5 can be prepared from the stable form, $\text{H-Nb}_2\text{O}_5$ (Fig. 1a), by deliberate doping with foreign ions. In preparing the so-called $\text{M-Nb}_2\text{O}_5$ modification by the method described by Emmenegger⁸, using chemical vapour transport in the presence of SnO_2 , we recovered the bulk of the feedstock as transported crystals of the stable $\text{H-Nb}_2\text{O}_5$. These had the domain structure described, with zigzag walls of intersecting defects (Fig. 2) lying on (100) and (001) orientations. A detailed analysis of one region is shown in Fig. 3: this matches the lattice image in dimensions at all points. In place of a row of (4×3) columns and tetrahedral sites, the (100) walls arise from insertion of an additional ribbon of linked (5×3) columns, X; they have the composition $\text{M}_{15}\text{O}_{37}$ ($\text{MO}_{2.4667}$). Two alternative structures are found on (001): folded ribbons of (5×3) columns (without tetrahedral sites), having the stoichiometry $\text{M}_{55}\text{O}_{136}$ ($\text{MO}_{2.4727}$), as at Y, and (4×3) columns (Z) so linked to their neighbours as to build up a strip of the $\text{M}_{25}\text{O}_{62}$ structure ($\text{MO}_{2.480}$). Occasional short segments of $\text{M}_{22}\text{O}_{54}$ structure ($\text{MO}_{2.4454}$) can be recognized. All these domain wall structures are substoichiometric: niobium must be replaced in part by atoms of lower valence. Having regard to the preparative method, we infer that Sn^{4+} is incorporated, concentrated and segregated in the domain walls. It will be noted that a

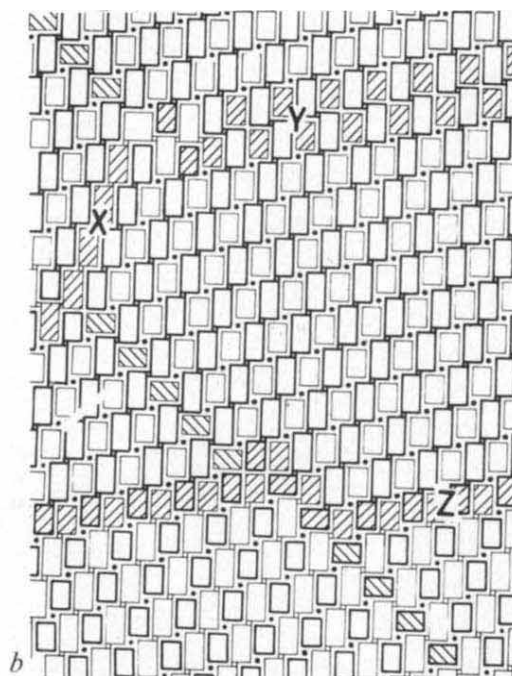
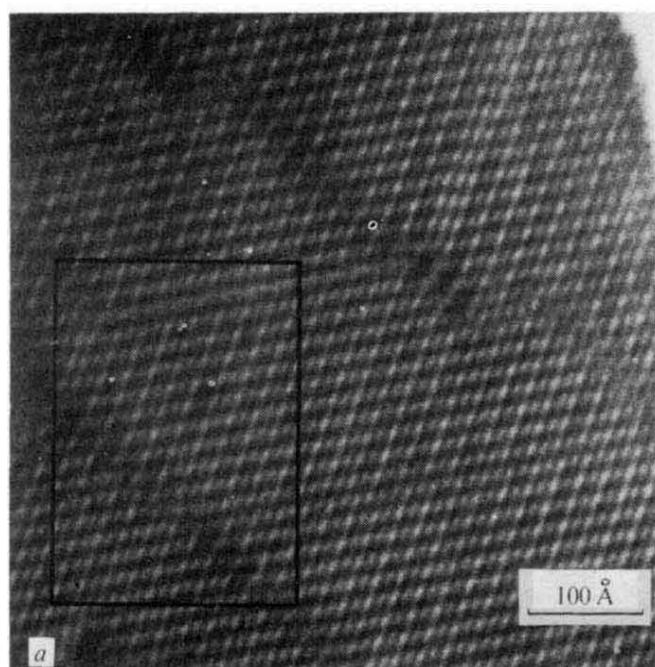


Fig. 3 a, Enlargement of one section from Fig. 2 ($\times 3,000,000$); b, complete analysis of the column structure within the area outlined, showing the structure of the domain walls (shaded). ▨, Stoichiometric extended defect; ▩, nonstoichiometric extended defect.

third defect, on $(10\bar{1})$ orientation, runs off from each intersection of the (100) and (001) domain walls. This is a stoichiometric defect, in essence a single strip of twinned orientation.

N-Nb₂O₅

This metastable form is known to be stabilized in presence of fluoride ion. We have obtained excellently ordered N-Nb₂O₅ (Fig. 1b) as a by-product of the preparation of MgNb₁₄O₃₅F₂ (a structure built from ribbons of (5×3) columns at both levels), from which it was formed by volatilization and loss of MgF₂. The crystals had a domain structure, with walls of wrong-sized columns on three orientations (Fig. 4). An analysis of one region is shown in Fig. 5b. Walls of (4×3) columns on (001) of N-Nb₂O₅ (A) constitute elements of M_{2.5}O_{6.2} structure; ribbons of linked (5×3) columns on (100) (B) are elements of M_{1.5}O_{3.7} structure; ribbons of linked (5×3) columns on $(10\bar{1})$ (C) are elements of M_{1.5}O_{3.7} (MO_{2.4667}) structure. The (100) faults are isostructural with MgNb₁₄O₃₅F₂ and undoubtedly represent the ordered segregation of both Mg²⁺ and F⁻. The (001) and $(10\bar{1})$ walls are both substoichiometric, and can be interpreted as having Mg²⁺ locally substituted for Nb⁵⁺. The intersection of two domain wall faults necessarily generates a third defect, which, in this case, may be either a twin boundary or a single linear extended defect, a 'tunnel with tetrahedral sites, extending along the b direction of the crystal, as at D.

Although the domain structures can be analysed only where they are revealed in detail, at the thin edges of fracture fragments, the network of walls runs continuously into the thicker parts of those fragments, in which the details of column structure are not resolved. They appear to be an integral part of the microstructure of the crystals. It is not certain how crystals of this kind grow by chemical vapour transport reactions; they form highly elongated needles, suggesting that the b axis is the direction of rapid growth and that successive (010) sheets are laid down, as on a template. Two possible processes for segregation of impurity atoms can be suggested. The first is that impurity atoms are rejected by an advancing crystallization front in a mobile surface layer. Their concentration then rises ahead of the growth front until it reaches a value that enables a suitable ternary oxide structure to be laid down, coherent because it is of the same general structural type as the host crystal. Alternatively, the domain wall structure might be formed preferentially, and then acts as a template which steers the subsequent course of crystallization. The source of material in the mobile layer would be depleted of impurity atoms, but the lamella of the ternary oxide would establish certain geometrical constraints on the sizes of columns

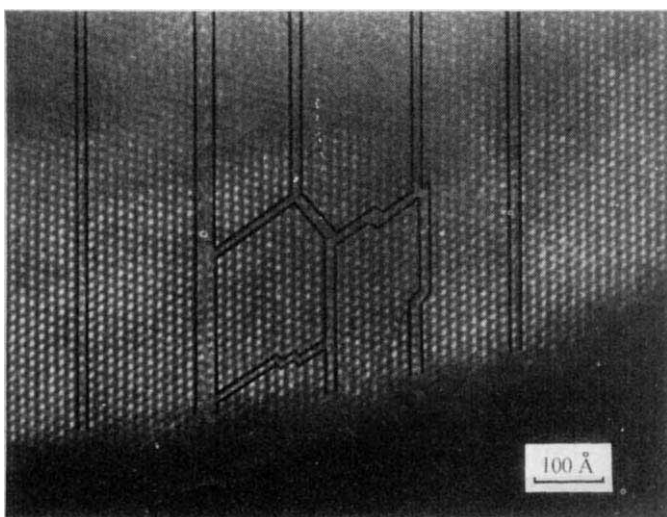


Fig. 4 Lattice image of N-Nb₂O₅, in dark field, showing domain walls.

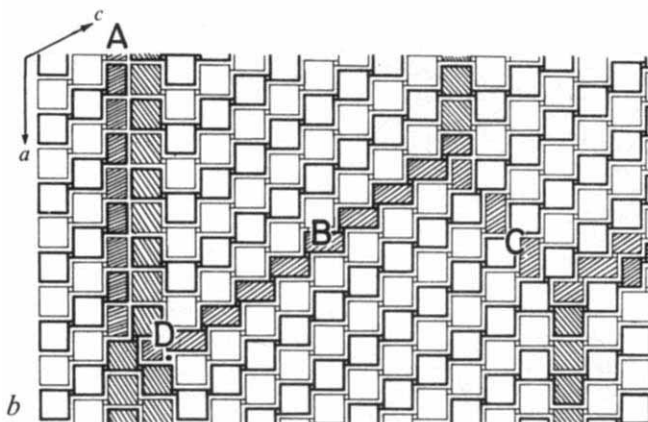
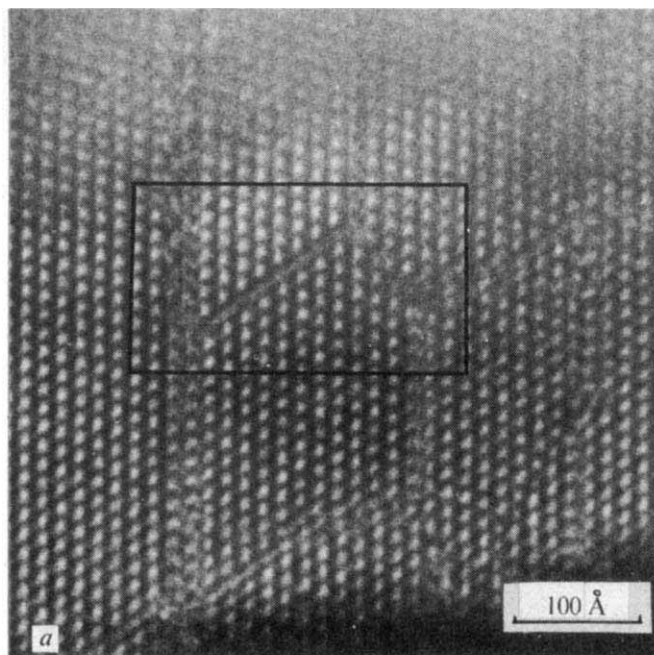


Fig. 5 a, Enlargement of one section from Fig. 4 ($\times 3,000,000$); b, analysis of the area outlined, showing column structure of the domain walls (shaded). ■, Stoichiometric extended defect; ▨, nonstoichiometric extended defect.

that could be coherently built on, and might thereby control the deposition of metastable modifications.

Finally, it may be pointed out that the effects described here bear a close similarity to the phenomenon of nonconservative crystallographic shear in simple oxide structures, such as rutile, WO₃ or MoO₃. There is a virtual uphill diffusion of altrivalent ions and point defects, and a readjustment of the way coordination octahedra are joined; a sheet of anion sites is eliminated, creating a planar singularity, and point defects are also eliminated. The planar faults considered here and in in other papers can, indeed, be described as resulting from crystallographic shear operations on the relatively complex parent structures.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Limits to the Sub-millimetre Isotropic Background

A PHASE-MODULATED Michelson interferometer¹ and a helium cooled Rollin² photoconductive far infrared detector, at the focus of a 35 cm aperture Cassegrain telescope, were flown at a height of 12.1 km from the Royal Aircraft Establishment, Farnborough, in a Comet 2E aircraft, on November 11, 12 and 16, 1971. The emission spectrum of the stratosphere was obtained in the wavenumber range from 36 cm^{-1} to 5 cm^{-1} (wavelengths $280\text{ }\mu\text{m}$ to 2 mm)³. Here we describe an analysis of a portion of this spectrum for features produced by sources outside the Earth's atmosphere.

Fig. 1 Phase modulation interferogram analogue plot of detector output against effective mirror separation. The signal to noise ratio lies between $10^3:1$ and $2 \times 10^3:1$.

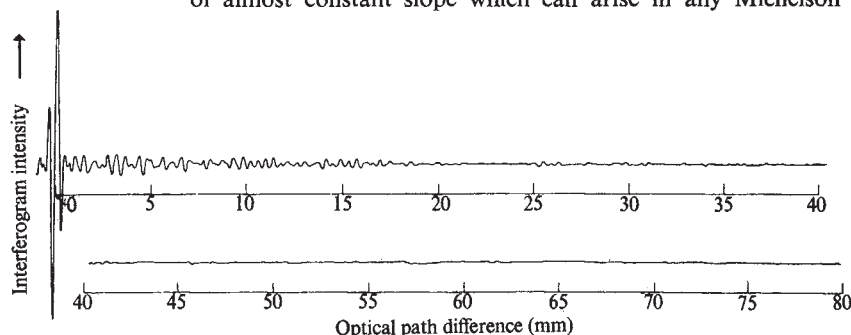


Fig. 1 shows an interferogram of a single run, of duration 30 min, from which we computed a spectrum covering the range to 36 cm^{-1} with an unapodized resolution of 0.0625 cm^{-1} . All the deviations from a level straight line in the wing repre-

sent spectral information, the signal to noise ratio being more than $1,000:1$. The elevation angle for this, and all subsequent runs but one, was 15° above the horizon, with a fixed cone semi-angle of acceptance for radiation of 1° on the sky. Fig. 2 presents a comparison of two separate transformed spectra, taken on November 12, when the tropopause was at a height of 11.4 km, demonstrating the reproducibility of even the weakest features. The baseline in the emission representation used here is defined by several instrumental effects, which have not been removed. One is the curved envelope caused both by interference in the beamsplitter of the interferometer and by the amplitude of the phase modulation; another is a sinusoidal variation particularly at the low frequency end of the envelope, of period 1 cm^{-1} , resulting from interference in the window of the detector, and the third is a "negative emission" contribution of almost constant slope which can arise in any Michelson

interferometer, because the detector "sees" a contribution from itself and its immediate surroundings—which include a metal cryostat wall at room temperature—superposed on the incoming beam but 180° out of phase. Also shown in Fig. 2

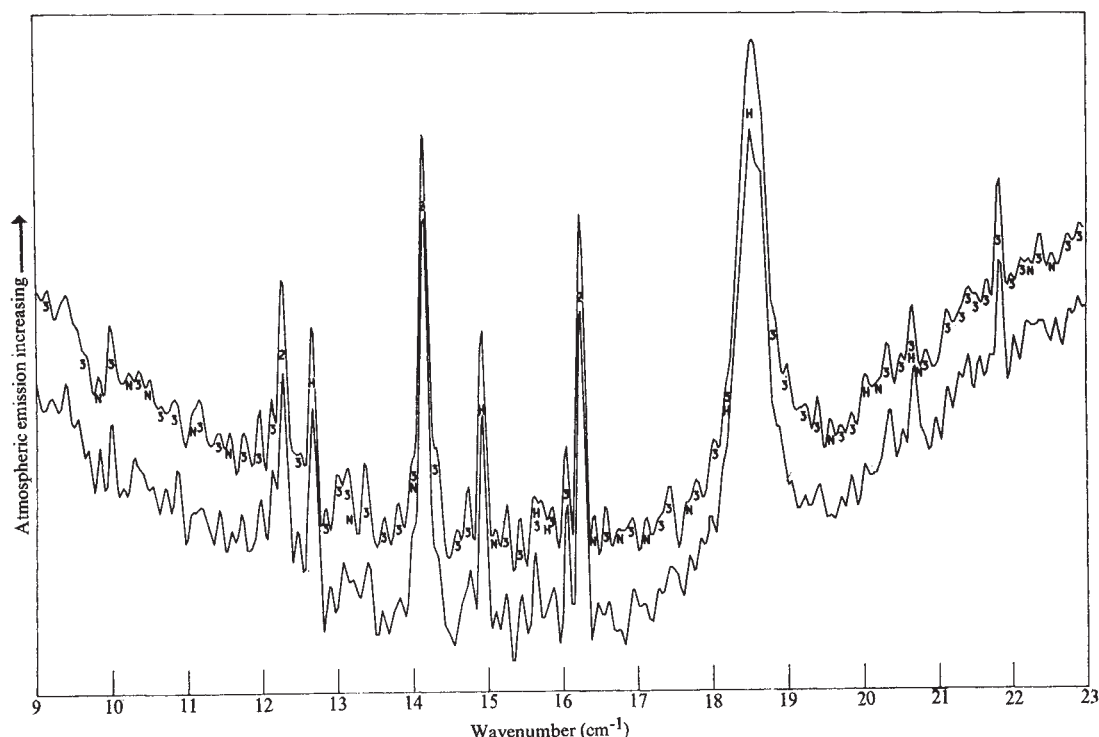


Fig. 2 Comparison of two independent spectra, both taken on December 12, 1971, each using a 28 min run time for 77 mm mirror separation to give 0.0067 cm^{-1} unapodized resolution. These spectra illustrate the reproducibility of the features, and may be used for identification. (H= H_2O ; 2= O_2 ; 3= O_3 ; N= HNO_3 .)

are the identifications of the observed line features which will be treated in detail elsewhere (Harries and Beckman, in preparation). Of these lines the weak ones are important here, being the key to our photometry; good agreements were found³ for positions and strengths of O₃ lines with theoretical spectra⁴, and for HNO₃ lines with laboratory data⁵ and near infrared atmospheric studies⁶. By a careful consideration of the fluxes in these weak features we are able to set an upper limit to any radiation in the form of emission lines which may be penetrating to 12.1 km from outside the atmosphere.

Changes of flight altitude and of elevation angle affected our spectra. Fig. 3a shows the effect of using an elevation angle of 40° at our highest altitude of 12.1 km. It was not possible to maintain the aircraft bank at the steady 25° from horizontal to obtain a run for the 30 min needed to produce 1/16 cm⁻¹ resolution, so only 1/7 cm⁻¹ resolution was achieved. Similarly we took an interferogram while the aircraft was rising between 8 and 10 km, with time only for the limited resolution of 1/6 cm⁻¹. Nevertheless these spectra show qualitatively the rapid changes in the strengths of the lines as a result of variations in the optical emission path. This is particularly clear in the case of the 18.67 cm⁻¹ water vapour line, and enables an estimate to be made of emission in the wings of this line, and the other strong lines, during photometric analysis of Fig. 4. This figure shows a spectrum on a scale of equivalent atmospheric transmission. In order to estimate the flux observed in the smallest reproducible features, and to set an upper limit to any extra-atmospheric line or continuum radiation, the emission spectrum of a real atmosphere may be related to the equivalent transmission spectrum through the relation⁷

$$E_v \propto (1 - T_v) \quad (1)$$

where E_v is the fractional emittance, and T_v the fractional transmittance at v , if the atmospheric path is replaced by a

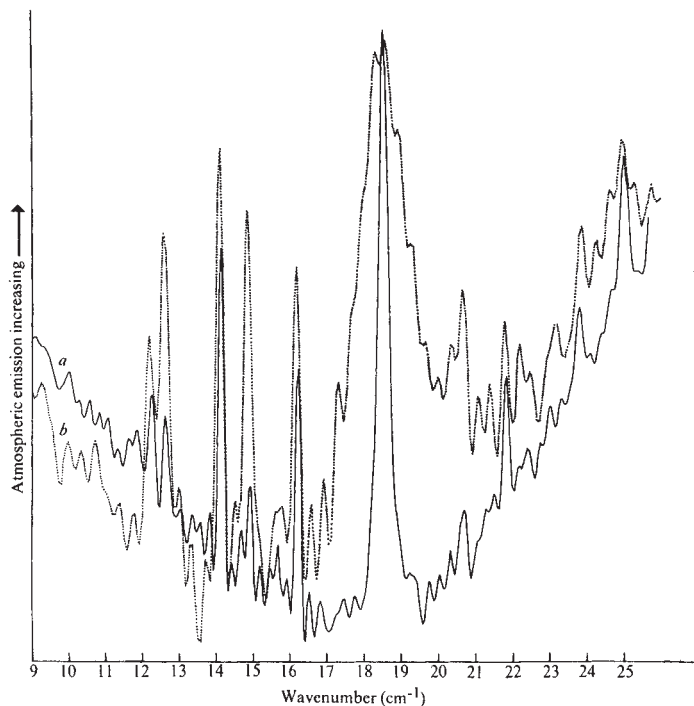


Fig. 3 *a*, "Banking" spectrum showing reduction of emission in all the observed lines, compared with the standard runs in Fig. 2. Although not as well resolved, this spectrum suggests that all the lines shown here are stratospheric. Altitude, 12.1 km; elevation angle, 40°; resolution, 0.125 cm⁻¹. *b*, "Rising" spectrum showing increased emission above Fig. 2 (standard), particularly obvious in the 18.67 cm⁻¹ H₂O line. Slight spectral shifts are due to variation in signal level as the aircraft rose. As all the data here were obtained above 29,000 feet, this spectrum shows the difficulty of using data from ground level for background photometry. Altitude, 8–10 km; elevation angle, 15°; resolution, 0.167 cm⁻¹.

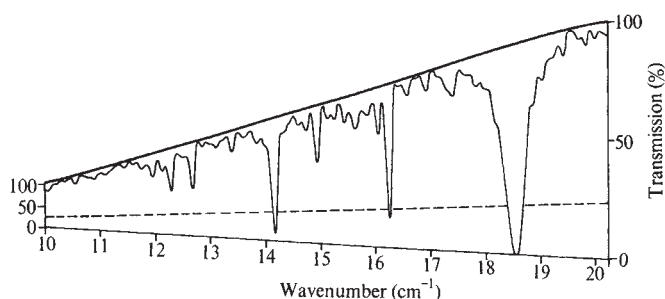


Fig. 4 Photometrically calibrated average of two spectra taken on November 11, 1971, resolution 0.0667 cm⁻¹. The upper envelope represents zero emission, the lower envelope zero transmission, and a brightness temperature close to 230 K throughout the given spectral range. All 100% ordinates on the photometric projection are normalized to 230 K. The dashed level represents zero net radiation exchange.

suitably scaled homogeneous atmosphere. The unconventional shape of Fig. 4 arises because of the contribution to the net signal seen at the detector, of the reflected anti-phase signal. The transmission scale shown in the figure depends on the total opacity of the 18.67 cm⁻¹ line of H₂O at its centre. The transmission of the equivalent homogeneous atmospheric path is zero (equation (1)). This defines the "zero atmospheric transmission" curve at one point. The ratio r of the ordinates at this frequency, above and below the dashed zero level, was then measured. The upper curve, corresponding to 100% atmospheric transmission, was then drawn through those windows where no, or only very weak lines, exist and the ratio r was used to evolve the corresponding lower line, of zero transmission. The transmissions in the peaks of other emission lines, defined on this scale, were then measured and agreement with the calculated values was good, supporting the validity of the construction.

The 100% atmospheric transmission line is curved downward above 19 cm⁻¹ because of the effects of the beam splitter and phase-modulation transmission characteristics. At the low frequency end, the curve exhibits a very shallow upward curvature; this is probably the v^2 (blackbody) dependence of the anti-phase radiation from the detector, but could also be due in part to any emission reaching the system from the cosmic background, at around 3 K.

The shape of the zero and 100% atmospheric transmission curves was also checked by recording spectra due to a black-body source⁸ in the laboratory at two temperatures, 288 K and 77 K. We also used these measurements to remove the interference fringes formed in the detector window.

The scale of equivalent atmospheric transmission in Fig. 4 may be interpreted in terms of effective sky temperature. At 18.67 cm⁻¹ the effective brightness temperature is near 230 K, the average temperature of the stratosphere. The 100% atmospheric transmission curve corresponds to radiation from the cosmic background, together with any residual emission from the atmosphere, plus radiation from any other extra-atmospheric sources. As shown here, the residual brightness temperature between pairs of weak lines cannot be greater than 6 K anywhere in this portion of the spectrum. The effective temperature of the zero of net radiation was determined from our laboratory work to be close to 150 K.

The atmospheric concentration data required for a quantitative analysis were obtained as follows. The Meteorological Office supplied a total ozone abundance value of 0.3 cm amagat; a value of 0.231 for the mass mixing ratio of O₂ was taken from the literature⁹, and a value of 2.5×10^{-6} for the mass mixing ratio of H₂O was measured from our previous results¹⁰. As an example showing the calculation of the flux in an observed weak emission line, we consider the line due to O₃ at 13.42 cm⁻¹. From Fig. 4, the measured equivalent width W_e of the line is 0.0025 cm⁻¹, using the upper envelope as a base line indicating zero line emission. Although the weak ozone lines

are certainly not instrumentally resolved, we can see that errors in equivalent widths are small. We now turn to a theoretical approach and, using the simple formula for the equivalent width of an unsaturated line,

$$W_v = S_v \eta \omega \quad (2)$$

where S is the integrated absorption coefficient, η the geometrical factor arising from our slant path through the ozone layer, and ω the abundance of O_3 . For the latter we use the figure already quoted, while η , the secant of the zenith angle, is 3.82. The value of S_v is found from Gora's work⁴, which gives the peak absorption coefficient α_v , and the pressure broadened half-width $\delta\sigma$, from the relation

$$S_v = \pi \alpha_v \delta\sigma \quad (3)$$

For this line, formed at a mean temperature of 230 K and mean pressure of 0.018 atm, the value of S_v is 1.88×10^{-3} cm amagat, and using the quoted values for η and σ we calculate an equivalent width for the line of 0.0022 cm⁻¹, in good agreement with the observation. Table 1 gives the observed and calculated equivalent line widths for a sample of the O_3 lines throughout the spectrum, chosen so that the line or O_3 blend is fairly clearly not blended with a much stronger line in each case.

Table 1 Observed and Calculated Equivalent Line Widths

ν (cm ⁻¹)	W_{th} (cm ⁻¹)	W_{obs} (cm ⁻¹)
12.16	0.0017	0.0015 *
13.42	0.0022	0.0025
13.62	0.0013	0.0015
13.82	0.0023	0.0020 *
16.03	0.0020	
16.05	0.0013	0.0055 *†
16.06	0.0030	
17.35	0.0030	0.0040 *
20.35	0.0034	0.0065 *†
20.38	0.0024	
20.70	0.0021	0.0060 *†
20.71	0.0032	
20.81	0.0018	0.0015
22.20	0.0025	0.0040 *†
22.23	0.0012	
22.34	0.0031	0.0035 *
22.40	0.0026	0.0030

* O_3 line is blended with another weak line.

† Equivalent width of blend of several O_3 lines.

The equivalent widths may be converted to a flux in emission, using the expression

$$\delta F_v = 2ck T v^2 W_v \quad (4)$$

obtained on the assumption that the ozone lines are in LTE with the atmospheric sub-millimetre flux, and that a black spectrum would form a Rayleigh-Jeans envelope; ν and W_v are in cm⁻¹ and T in K (we can take $T=230$ K). For the ozone line at 13.42 cm⁻¹, δF_v is 1.7×10^{-11} watt cm⁻² sr⁻¹; this also represents the approximate size for the flux of a single line which would just be detectable through the distribution of emission lines seen in our spectra more than one wave number away from the centres of the strongest lines. This flux is equivalent to less than one fifth of the total flux received outside the atmosphere from an isotropic background radiating at a temperature of 2.7 K.

In 1968 the NRL-Cornell group¹¹ using rocket-borne broadband detectors found a sizable excess F_e in the sub-millimetre range, between 7.5 cm⁻¹ and 25 cm⁻¹, of 1.3×10^{-9} watt cm⁻² sr⁻¹ above that expected from a 2.7 K radiation field which, if it represented a departure from the continuum of the 2.7 K Planck curve, would be of great importance in cosmology. Muehlner and Weiss¹², however, using balloon borne equip-

ment of somewhat better spectral resolution, obtained a differential spectrum consistent with a 2.7 K background on which a strong emission feature which must lie between 10 and 12 cm⁻¹ is superposed. Our results clearly preclude such a feature, which would appear in the spectra as a line of similar equivalent width to the H_2O line at 18.67 cm⁻¹, one of the strongest lines presented on our spectra. There is nowhere within our range where such a major line, to contain an F_e of thirteen times the total flux from a 2.7 K field, could be hidden by atmospheric absorption, even if the line were to coincide with a strong feature due to H_2O or O_2 .

More recently Beery *et al.*¹³ reported a narrow emission line at 11.7 cm⁻¹ in spectra obtained from 13,600 feet altitude at Mauna Kea, which, if not accounted for by any atmospheric component, could explain the excess of rocket and balloon observations. Our spectra show no such feature, thus indicating at best its origin in the lower atmosphere. This would appear to be ruled out by the results of Mather *et al.*¹⁴, obtained from White Mountain at 12,500 feet altitude, and by data from the Pic du Midi, at 10,000 feet (P. A. R. A. and P. E. Clegg, private communication), each showing spectra without a line at 11.7 cm⁻¹. In each case the observers' spectral resolution of better than 0.1 cm⁻¹ and their measured low values for the atmospheric H_2O paths should have ensured a detection. We thus confirm these findings, and reject the explanation of any sub-millimetre excess in terms of a single strong extra-terrestrial emission line between 10 cm⁻¹ and 12 cm⁻¹.

In spite of the limitations to photometric accuracy in the continuum manifested in Fig. 4, our results set a fairly well defined limit to the spectral width of any sub-millimetre excess there might be, in the form of a broadly peaked emission feature. If the line corresponding to 100% transmission in Fig. 4 were displaced by 2% of its ordinate value above any of the O_3 features tabulated in Table 1, the measured equivalent widths would double in value. It would then be very easy by comparison with our theoretical values to detect a 2% excursion anywhere between 10 cm⁻¹ and 20 cm⁻¹, such as would occur if an otherwise undetected broad feature were superposed. In fact, from the lines alone, we estimate that a 0.5% departure would be detectable but a further 1.5% to 2% uncertainty in the shape of the interferometer envelope caused by phase modulation hooping makes our conclusion markedly less powerful. Only a better calibrated system, using a different method of amplitude division in the interferometer, could improve significantly on this degree of photometric accuracy. Our conservative figure of 2.5% amounts to an incremental brightness temperature ΔT_B of 5.8 K. If we may assume that a sub-millimetre excess takes the form of a symmetrical triangular function, then its half-width ν is related to its peak incremental brightness temperature ΔT_B and the excess flux δF by

$$\delta F = 2ck \Delta T_B \nu^2 \Delta \nu \quad (5)$$

so, using for δF the value $F_e = 10^{-9}$ watt cm⁻² sr⁻¹, we obtain $\nu_{min} = 3$ cm⁻¹ for a line peaking at 11 cm⁻¹. Any significantly narrower feature would be detected. A repetition of the experiment directed more specifically at establishing the continuum could measure values of ΔT_B down by a factor of 3 on the present value, though this would also require a spectrometer to be flown somewhat higher, say, at 13.5 km with a lower tropopause, to avoid more of the water vapour, and with the ability to go to smaller zenith angles.

We conclude that any sub-millimetre extra-atmospheric excess of flux, of magnitude 10^{-9} watt cm⁻² sr⁻¹ or greater cannot be reconciled with the data presented, anywhere between 10 cm⁻¹ and 25 cm⁻¹, unless it takes the form of a very broad feature, of half-width greater than 3 cm⁻¹. No single narrow line can contribute more than 2×10^{-11} watt cm⁻² sr⁻¹, unless it coincides with one of the principal atmospheric features. The upper limit to the radiation which could be hidden by absorption in such a feature is 4×10^{-10} watt cm⁻² sr⁻¹; this would have to be in the H_2O line at 18.67 cm⁻¹, and not in agreement with the location of any excess claimed by

previous observers. The upper limit to the flux available in lines which appear as very weak features in our spectra but are as yet unidentified is 10^{-10} watt cm^{-2} sr^{-1} , and there is a fair prospect of obtaining identifications for some of these in terms of minor constituents such as H_2SO_4 . Our results are thus in complete agreement with those of Blair *et al.*¹⁵ in which a rocket borne radiometer detector observed a flux of 1.5×10^{-10} watt cm^{-2} sr^{-1} between 6 mm and 0.08 mm equivalent to a background temperature of $3.1(^{+0.5}_{-2.0})$ K. It is extremely difficult to reconcile our data with an effective background temperature of more than 6 K, and taken together with the result of Blair *et al.* they suggest that there is no current observational evidence that the isotropic background radiation presents other than a 3 K blackbody continuum. A more powerful result can be obtained by flying a similar spectrometer at balloon altitudes, say, 30 km, when one might hope to follow a 2.7 K continuum at both sides of the intensity maximum. When such an experiment is performed, the line spectral data presented here will be of value in distinguishing the atmospheric from extra-atmospheric radiation.

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Radiation from Flares near the Magnetic Poles of Pulsars

It is generally accepted that pulsar emission is produced by material ejected from the surface of rotating neutron stars near the magnetic poles. The charged particles are thought to radiate as they are accelerated along magnetic field lines or as they approach the "speed of light cylinder". But the exact mechanisms by which emission is produced over the full range of the spectrum from gamma rays to radio frequencies^{1,2} are not understood.

I wish to point out that this radiation could be produced by the flare mechanism proposed^{3,4} to explain solar observations. The way in which energy is released in solar flares is still not understood but the events occur close to sunspots where magnetic field lines emerge from the surface of the Sun. The field geometry is similar near the magnetic poles of neutron stars, which suggests that this same model could apply to that region. Emission from a flare on a neutron star will be highly directional, so radiation will be observed at the Earth during part of each rotation only, thus giving rise to the characteristic pulses.

In the model, it is assumed that the flare energy is stored as a current flowing along the magnetic field lines emerging from the surface of the star. I shall show later that currents are induced as a result of stellar rotation, but first I shall explain how the electromagnetic spectrum can be produced. I consider the case of NP 0532 although parameters may well be incorrect by more than an order of magnitude. The energy emitted per rotation is $\sim 10^{28}$ J. For reasons which will become clearer when the structure of the active region is discussed, a single flare may emit considerably less than this: I assume 10^{27} J for these calculations. This energy must be stored in an "electrical circuit" defined by the magnetic field lines. The length L of the conducting region should be within the range 10^4 m to 10^6 m, determined by the diameter of the pulsar and the distance to the speed of light cylinder. Choosing 10^5 m for this study, the self inductance $\mu_0 L/(8\pi)$ is $\sim 10^{-2}$ H when only magnetic flux within the current channel is considered. The energy E (10^{27} J) would be stored if the current was greater than 5×10^{14} A because $E = LI^2/2$, but I assume that the current increases rapidly from zero until this value is reached as a result of rotation of the star.

For the solar case, Alfvén and Carlqvist³ explained how the flow of current might be interrupted as an instability develops when the drift velocity equals the thermal velocity of the plasma carrying it. A feature of NP 0532 to be discussed later suggests that the current interruption might occur as the pinch effect becomes significant; but whatever the cause, the energy stored has to be dissipated as the current decays. This results in a build-up of potential $L dI/dt$ across the instability.

The time taken for the current to decay is determined by the speed at which energy can be transported along the magnetic field lines to the instability. This cannot be calculated accurately unless the particle density along the path is known⁴. But the lifetime of each individual flare cannot be much greater than the rotation period of the star (which means that flares will have to recur in the same region) because large variations in intensity are observed between pulses⁵. On the other hand, the lifetime will not be shorter than the width of a single pulse, which suggests a decay time of the order of 30 ms for the current, in which case the potential set-up is 2×10^{14} V.

My principal aim is to describe how the extended electromagnetic spectrum can arise at a disruption of the current. Nevertheless, sufficient is known about the nature of the source, such as its small dimensions and its proximity to a magnetic pole, for it to be necessary to discuss how it might arise on the star. Because the size of the instability is determined by the diameter of the current channel, it is necessary to determine where a high current density can arise with a small cross-sectional area. It is implicit in Maxwell's equations

that a current is produced when magnetic field lines are twisted, so the location of the source might be inferred by examining how the general field of the body is distorted during rotation of the star. Sturrock⁶ has described how open field lines emerging from the magnetic poles should be anchored in the region of the velocity of light cylinder. As a result they become twisted because the opposite ends move with the polar region. There will be a shear between the limiting open lines and the limiting closed field lines which rotate with the body, so there must be a thin region with high current density at this outer edge of the magnetic polar cap. But Sturrock assumed that there would be a current sheet at the interface, whereas it seems possible that this might be an unstable configuration.

I will assume that the magnetic field lines at the boundary become twisted into numerous "magnetic ropes" because of the relative motions of the open and closed field lines. It can be visualized that as the open and closed field lines move, the sliding motion between the two boundaries is "lubricated" by a rolling of the field lines into a spiral structure within a narrow intermediate region. Although the open field lines receive one extra twist per rotation of the star, the lines within the boundary region will be twisted once each time the open field lines slide across the closed lines by a distance equal to the circumference of the "rope". Twisting of each rope will therefore take place very rapidly until the current density reaches a limit at which the instability which releases the energy occurs. Flares will therefore be located on the ring which defines the edge of the magnetic polar cap from which the open field lines emerge. It seems probable that such events will occur where the current density is highest; that is, near the surface of the star where the current channel has its smallest diameter. After each flare the current will begin to increase again so that at any instant there might be many separate flares active around each magnetic pole. Not all of these flares will be visible during one rotation of the star, however, because in general the cone within which radiation is emitted will not intersect the prospective observer. The magnitude of each observed pulse will therefore be determined by the stage of development of suitably located flares active at the instant of observation. The integrated pulse envelope will be determined by the location of the observed flares on the polar cap boundary. The emitting regions are therefore located as described by Sturrock⁶ but the radiation mechanism differs from that of his model.

In all pulsar models it is necessary to explain how charged particles become bunched so that the emission is coherent. It seems that conditions are particularly favourable in this model because the instability occurs in a boundary layer which is very thin compared with the radius of the neutron star. I have not yet determined whether the individual current channels can have a diameter as small as 1 m, as suggested by the coherence of radio waves. But they cannot be much smaller than this because the toroidal magnetic field ($\mu_0 I/\pi d$) associated with a current of 5×10^{14} A in a channel of diameter $d=1$ m is $\sim 10^8$ Wb/m² and is therefore similar to the field of the neutron star. This suggests that conditions might be close to pinch instability.

The length of the instability is also small. Carlqvist⁴ has shown that for the conditions considered above, the length is ~ 10 m. Charged particles which produce the pulsar emission will be accelerated in the electric field of $\sim 2 \times 10^{13}$ V/m, although there will be considerable continuous energy loss caused by synchrotron radiation from both electrons and protons. As an example, I assume that because of "misalignment" of the electric and magnetic fields, or because of curvature of fields, the component of the magnetic field perpendicular to the trajectories of the particles is 10^6 Wb/m². Electrons will reach a limiting energy of approximately 10^8 eV while protons will gain a final energy close to 10^{14} eV. Emission from electrons will be in the gamma and X-ray range while radio emission will be produced by the protons. The spectral range is determined by the ratio of the magnetic field of the star to the electric field produced. In the case con-

sidered, the electrons are sufficiently energetic to produce X-rays, but in other sources the electrons may be barely relativistic.

Because the energy loss rate in the magnetic field is so great, energetic particles produced by this mechanism will only exist in the electric field region. All charged particles will therefore be extremely well collimated in the direction of the electric field; so emission should be highly polarized. As a result, radiation should be observed only when the particles are travelling towards the observer.

Many features of pulsar emission are explained by this model. Electric fields with strengths greater than 10^{13} V/m might be set up with dimensions of the order of metres close to the magnetic poles of neutron stars. Electrons and protons accelerated in the fields should emit synchrotron radiation over a considerable spectral range. Other features which are explained include the variation of emission between one pulse and the next and the occurrence of structure during single pulses if more than one flare is observed during a rotation of the star. I thank Professor R. L. F. Boyd, my colleagues in his group, Drs P. Carlqvist and M. J. Rees and many others for suggestions.

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Rotation of Lunar Dumbbell-shaped Globules during Formation

It is generally agreed that the glass globules found in type D lunar fines are ejecta from primary meteoric impacts. The impact is presumed to generate melted rock and gas, solidification of the ejecta occurring before they return to the lunar surface, but the precise manner of formation of the globules from the melt is uncertain. In particular, some globules are elongated with rotational symmetry about the major axis¹, but retain the smooth surface characteristic of the more common spheroidal globules².

There is some controversy about the mechanism of formation of these non-spherical shapes. One view is that the melt is ejected in jets which subsequently break up and solidify^{2,3}. The equilibrium shape from this process is the sphere; non-spherical shapes may be accounted for by supposing that the droplets congeal before they relax to the equilibrium shape. Others^{4,5} suggest that the ejecta are masses of melt which assume a regular elongated shape governed by the equilibrium between the opposing effects of surface tension and rotation of the globule. I wish to support the second viewpoint with some measurements.

The problem of computing the analytical form of the equilibrium shape of these globules (subject to opposing rotational and surface-tensional forces) is complex, and was not treated in the literature until recently⁵. But the surface curvature of globules can be computed from measurements made on photographs, and this can be compared with a simple equation⁴ which connects the total curvature G of the surface with surface tension S and angular velocity ω :

$$SG = p_0 + 1/2 \rho \omega^2 x^2 \quad (1)$$

where x is the distance from the rotational axis of the point at which G is determined, as shown in Fig. 1, ρ is the density of the material of the globule and p_0 , a constant of integration, is identified to be the pressure on the axis of rotation (the y axis of Fig. 1). The factor of $1/2$ in the last term of equation (1) appears to have been omitted in the original by Bastin and French⁴.

Measurements of the surface curvatures of several globules agree well with the rotation model. The comparison between theory and observation is shown in Fig. 2 in the case of one particular globule which has a marked dumbbell form. The most consistent method for measuring curvatures was found to be matching of the photograph to sample curves on a transparent overlay. To complete the computation of the curvature it is necessary to make an assumption about the shape of the globule perpendicular to the plane of the photograph. The simplest and most satisfactory assumption is that the globule possesses rotational symmetry about its long axis (x axis of Fig. 1). So far only eight globules have been examined in detail, largely because of difficulties in obtaining prints with sufficient definition.

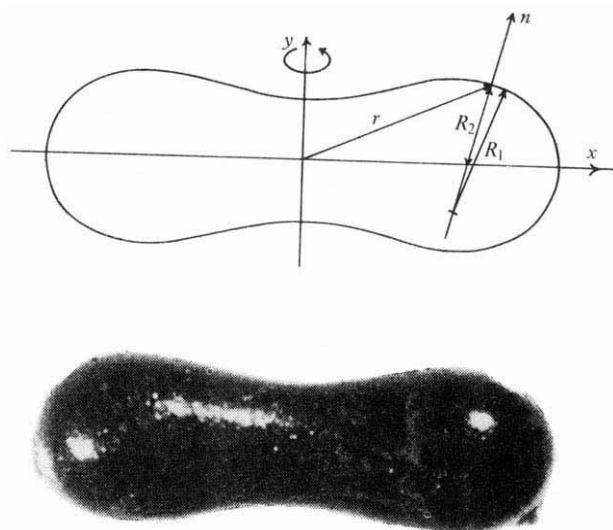


Fig. 1 A typical globule studied. Actual length just over 0.6 mm. Diagram identifies the axes of description, the radius x of equation (1), and the radii R_1 and R_2 , such that the curvature $G = R_1^{-1} + R_2^{-1}$. The globule is presumed to rotate about the y axis (original photograph by Max-Planck-Institut für Kernphysik).

Fig. 2 shows good agreement between the observations and the prediction of the rotating-globule model. It is interesting to look at the requirement that the globules possess angular momentum. Using typical values³ of ρ ($2.5 \times 10^3 \text{ kg m}^{-3}$) and S (0.3 J m^{-2}), appropriate to molten lunar glasses, and substituting from observation into equation (1), rotational speeds are found to be in the range 500–1,000 revolutions per second ($3\text{--}6 \times 10^3 \text{ radian s}^{-1}$). For any given shape higher speeds are observed, as required by theory, for smaller sizes. The “pressure” p_0 is found to be 30 mbar ($3 \times 10^3 \text{ N m}^{-2}$), also rising as linear dimensions are reduced.

Unlike the case of the formation of liquid droplets in an atmosphere, the mode of formation of the lunar globules immediately produces a mechanism for the production of high angular velocity. The velocity field of the ejecta covers all directions within the half-space above the lunar surface at the impact site, and all speeds from zero, at the crater edge, up to velocities lower than, but within an order of magnitude of, the velocity of the impacting meteorite, arising chiefly at the centre of the crater. The craters which dominate the properties of the lunar surface layer are those in the submetre size range.

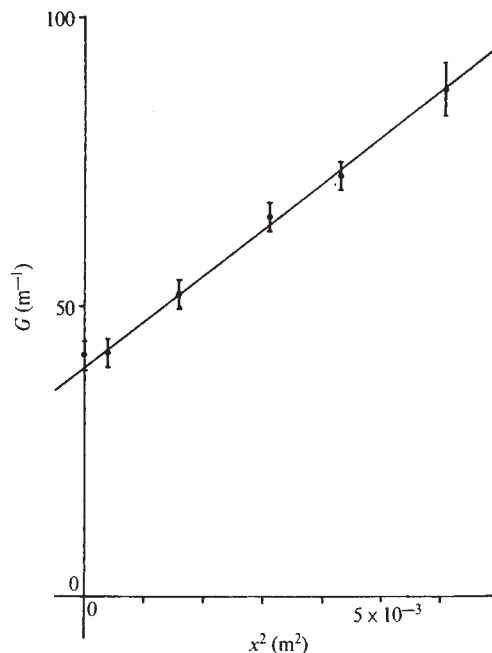


Fig. 2 The experimental points for the surface curvature of the globule in Fig. 1. The scales refer to the dimensions of the enlargement studied, which was found to be magnified $\times 260$.

One may interpret this velocity gradient as an angular velocity; as an estimate of this we divide the velocity difference between centre and edge of the crater by the radius of the crater. Hence the velocity range, 0 to 10^3 m s^{-1} , can be converted into an angular velocity range 10^3 to 10^4 s^{-1} , in agreement with the observation. Smaller-sized craters would be expected to be associated with even greater angular velocities, although large particles would then break up into smaller ones such that surface tension can provide the required centripetal force. The detail of this mechanism suggests that at small sizes of globule there is insufficient angular momentum to produce marked rotational forms. Hence, in the categories of shape listed by Mueller and Hinsch, we reproduce the observed fall off in relative abundance of the rotational shapes at small sizes.

Finally, we must consider and account for those glassy objects which, although smooth in surface form, do not possess an axis of symmetry. It is likely that these never melted completely, or achieved so low a temperature that surface tension forces did not overcome viscosity of the material before cooling caused the globule to solidify once more. It has already been shown^{3,4} that, in general, the time for relaxation to equilibrium shape is less than, but of the same order as, the time for cooling of the globule to a temperature at which it is essentially solid. Adjustment of the parameters in such calculations can reverse this position, and the detail figures are sensitive to the original assumptions, although remaining of the same order. Accordingly, we expect a proportion of irregular shapes to be present in the fines, as well as the regular equilibrium shapes investigated in this note.

I thank Professor J. A. Bastin for advice and discussions.

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Some Aspects of Precambrian Development in East Africa

THE development of the African continent is often considered as a progressive growth of the stable areas, or cratons. This growth was achieved through consolidation of mobile belts and geosynclines around eight primary cores or nuclei, older than 2,500 m.y. (ref. 1). The area of the ancient nuclei is small compared with that of the present African craton.

For other Precambrian shields, such as the Canadian Shield², it has been suggested that the stable areas grew around primary nuclei. But there is evidence that the process was reversed in East Africa during the Proterozoic, especially in the Upper Proterozoic.

It is now known that mobile belts (or Clifford's vestigeosynclines) developed widely in Africa and are formed mostly by old cratonic material (older than 2,500 m.y.) subjected to tectono-metamorphic rejuvenation at various times. Thus the Archaean rocks in the Limpopo belt, and probably those in the Ubendian-Ruzizian belt, were rejuvenated 2,000 to 1,800 m.y. ago; for those in the Namaqualand belt rejuvenation occurred 1,250 to 900 m.y. ago^{1,3}. Extensive areas in Eastern and North-Central Africa underwent the tectono-metamorphic rejuvenation during Damaran-Katangan orogeny (550 ± 100 m.y.). It seems that the largest mobile belt of this epoch—the Mozambique belt—is mostly built up of Archaean rocks, as emphasized by the wide distribution of granulite facies (shown in standard survey maps of Kenya and Tanzania, 1:125,000) uncommon in metamorphic complexes younger than Archaean. Direct transition from the Archaean granites of the Tanganyika and Rhodesia shields to the Mozambique gneisses has been established in a number of localities⁴⁻⁶. The Archaean Mozambique gneisses extend to the north as far as Ethiopia⁷.

Besides the older gneisses one can distinguish in the Mozambique belt some metasediments (quartzites, aroccoses, limestones and so on) which once formed a cover on the Archaean rocks. In Kenya they were recognized as the Turoka series⁶, which should probably be correlated with the graphite-limestone series of Tanzania⁸ and the Wadera series of southern Ethiopia⁷. The sediments were folded and metamorphosed together with the ancient basement during the Mozambique tectono-metamorphic event.

Since the ancient platform cover is older than Upper Proterozoic (in Ethiopia it acts as a "basement" for the Upper Proterozoic folded belts) and younger than Archaean, its age can be tentatively placed within Lower-Middle Proterozoic. It therefore appears roughly contemporaneous with the platform cover on the cratonic massifs of South Africa. Thus it is probable that in pre-Mozambique (or pre-Pan-African) time the belt was a part of a large Archaean craton together with what now constitutes the Tanganyika, Rhodesia and Kaapvaal cratons. Tectono-metamorphic activation of the old cratonic material led to the formation of the mobile belt which acted as a zone of weakness and instability during the later stages of the geological history. In Karroo time the Mozambique and Zambezi belts controlled the distribution of sedimentation troughs and volcanism. There is some evidence that the separation of Gondwana (or at least the separation of Madagascar from Africa) took place along the Mozambique belt⁹. The Tertiary-Quaternary rifts in East Africa also follow the pattern of the mobile belts, reflecting a new stage of disruption of the African continent.

Thus it is hard to accept that the formation of the Mozambique belt was a "cratonization"; on the contrary, it looks like the beginning of disruption of an ancient Archaean craton. A somewhat similar idea has already been expressed by Anhaeusser *et al.*³. If this conclusion is justified for other mobile belts, as is likely to be the case, the area of the Archaean protocraton could be very large.

One must also remember that many Upper Proterozoic folded belts in Africa (Kibarides, Katangides) are miogeo-

synclines apparently formed on the thick granito-gneissic crust. This is shown by the type of sedimentation (mainly terrigenous rocks) and specific character of magmatism (absence of ultrabasic and basic rocks). In some cases the underlying sialic crust could be either Archaean or rejuvenated Archaean, though this is not established.

The following succession of Precambrian events may be suggested at least for a larger part of South and East-Central Africa. First, formation of large Archaean craton (older than 2,500 m.y.); second, accumulation of platform cover over the great part of the craton (2,500–2,000 or 1,800 m.y.); third, development of the first mobile belts (Limpopo, Ubenda) marking the beginning of disruption of the protocraton (2,000–1,800 m.y.); fourth, large scale rejuvenation of the ancient basement in the Upper Proterozoic (younger than 1,600 m.y.). Formation of: (a) mobile belts (Mozambique, Zambezi, Namaqualand) and (b) miogeosynclines on the rejuvenated basement (Kibarides, Katangides).

The ancient massifs such as the Tanganyika, Rhodesia and Kaapvaal cratons should be considered not as nuclei but as the relics of a large Archaean craton.

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Major Strike-slip Fault of Late Hercynian Age in Morocco

IN Morocco, there are two main zones of Hercynian outcrops, one north and one south of the so-called "South Atlantic Fault"¹ (Fig. 1). In the southern part, the intensity of folding remains moderate, gradually decreasing southward towards the tabular platform of the Sahara Shield. By contrast, the northern part seems to be the heart of the folded belt: deformation is more marked, with an outstanding development of slaty cleavage and some metamorphism, with several intrusions of granitic plutons.

In the alpine zones of the Middle and High Atlas, these Hercynian units have been deformed again by Cainozoic tectonics, but not intensely enough to obliterate the Hercynian structures.

The principal features of the Hercynian tectonics in most massives are well known. Because of the widespread post-Hercynian deposits, however, only isolated blocks outcrop in this northern zone, so that the general pattern of the folds has not yet been settled. In this communication we show that, when attempting to restore the pattern of these Hercynian folds, one must take into account the existence of late Hercynian strike-slip faults which altered the original features; and we give a first outline of one of the most important of these strike-slip faults.

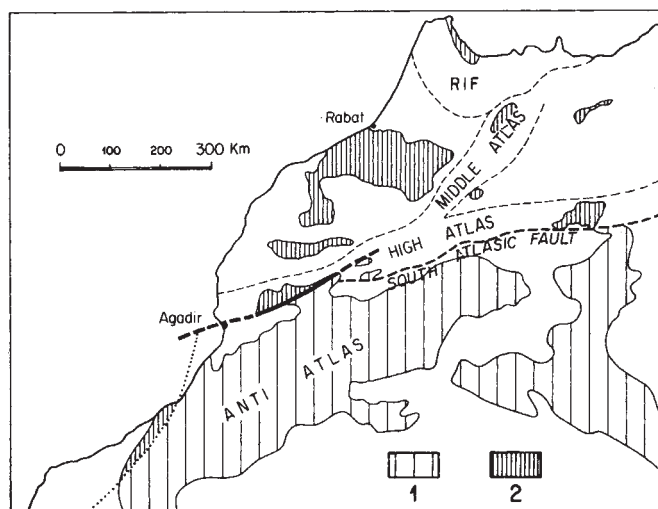


Fig. 1 Hercynian outcrops in Morocco and location of the Tizi n'Test strike-slip fault; intensity of the Hercynian folding: 1, moderate; 2, strong.

There is an important fault zone in the western part of the High Atlas¹. This appears clearly on the geological map of Morocco². It stretches from the Ida-ou-Zal Stephanian basin (north-west of Taroudannt), in a north-easterly direction to Ijoukak, running through the Tizi n'Test pass, and delineates the northern border of the High Atlas Precambrian massive ("Ouzellarh Headland"³), extending probably as far as the oued Rdat valley.

This fault-zone, which can be observed for roughly 200 km, affects not only Precambrian and Palaeozoic, but also Permo-triassic and Cretaceous formations. The post-Triassic slips can be seen in vertical displacements (possibly 4 km), which might explain why most structural studies have been devoted to post-Hercynian tectonics, rather than Hercynian tectonics, here Prepermo-triassic.

But, if one disregards these vertical movements which are due either to Permo-triassic "extension" or Tertiary reverse faulting, and studies the Hercynian formations on both sides of this main fault zone, one can see that the fault zone existed before the Permo-triassic, and that it entailed a large horizontal displacement. On the southern side, the folds in the lower Palaeozoic series are typically concentric, without cleavage. The folding has not been very strong and the beds are often

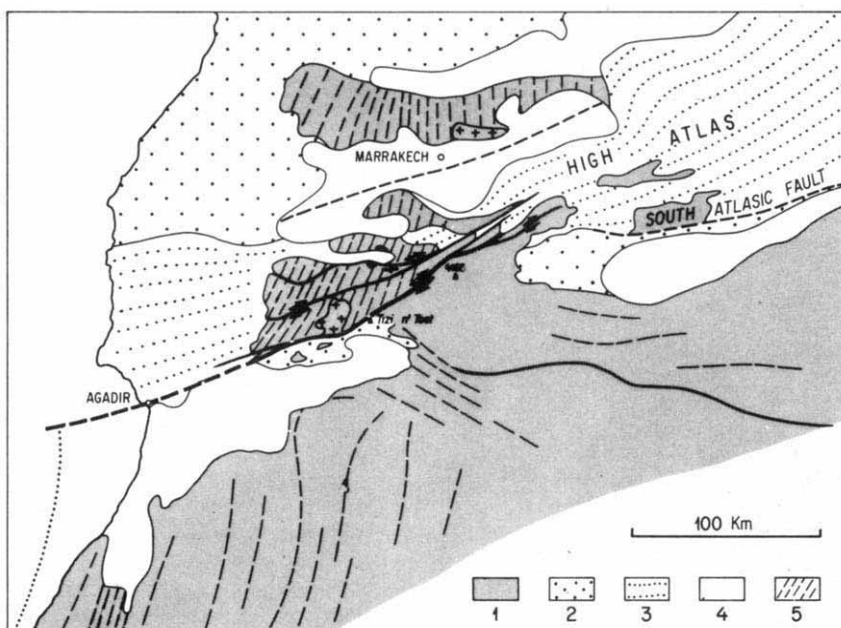
subhorizontal over large areas. On the northern side, by contrast, the same series is intensely folded^{5,6}, with obvious slaty cleavage. Also, the series is generally epimetamorphic and sometimes intruded by granites. Thus the northern part must have been "deep" (that is, it has been folded in a low "structural level"), whereas the southern part seems to be much more "superficial". Also, the strikes of the folded structures on each side are completely different: they run north-south in the north and close to north-west-south-east in the south. Both are abruptly intersected by the north-east-south-west fault zone. In these conditions, the Tizi n'Test fault must be regarded as a strike-slip fault, which caused contact between two very different segments of the Hercynian belt (Fig. 2).

This interpretation is consistent with detailed observations along the fault zone; for example, horizontal striations caused by horizontal movements on subvertical shear planes (slickensides). Of course, the existence of these horizontal striations in Prepermo-triassic beds is not sufficient evidence for their late Hercynian age. They could be marks of Tertiary or other recent movements. But such a Tertiary shifting of the Hercynian structures would be very difficult to conclude because of the following three reasons. First, at both ends, the Tizi n'Test strike-slip fault appears as Prepermo-triassic, the principal component of the post-Permian offset is generally vertical (normal or reverse) and the horizontal movements have been very slight; second, in the Permo-triassic blocks which are squeezed in the fault zone, there are very few horizontal striations; therefore, the slip must have been mainly vertical; third, all over the area under study, the observable strike-slip faults (horizontal striating) are mostly Prepermo-triassic.

Thus the major horizontal slip of the Tizi n'Test fault has been Prepermo-triassic and posterior to the Hercynian folding. Since the fault clearly affects (in the western Atlas) some formations of Stephanian⁷ and perhaps lower Permian age (which does not exclude a first Prestephanian slip), it actually appears as a late Hercynian fault.

This contrast between the types of folding on both sides of the strike-slip fault can be observed for roughly 100 km; therefore, the horizontal slip must be important. Of course its value will be different whether the fault is considered as contemporaneous with the folded structures or posterior to them. In the first case, this value would be related to the difference between north and south "shortenings" due to the difference in folding—about 40 km—and in the second case, it could reach up to a hundred kilometres. In our opinion, the first hypothesis is highly improbable, because the contact

Fig. 2 Structural map of the studied area showing the Tizi n'Test late Hercynian strike-slip fault and minor faults of the same type: 1, Palaeozoic; 2, Mesozoic and Cainozoic, unfolded; 3, folded; 4, quaternary; 5, approximate trends of folding.



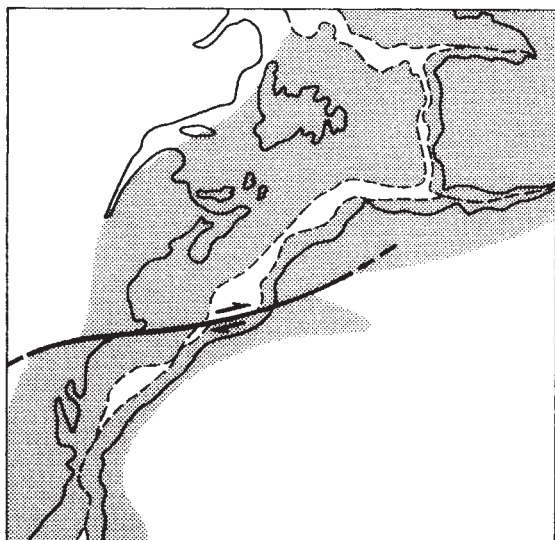


Fig. 3 Suggested extension of the Tizi n'Test strike-slip fault into the North American continent; shaded area indicating the Hercynian fold belt.

between the two domains is clear cut everywhere, and the trends of the fold axes are quite different.

On a larger scale (Hercynian folding in all of Morocco), it seems that the Tizi n'Test fault should be regarded as a right lateral strike-slip fault, the slip of which could possibly extend for 200 km. Indeed, south of this fault, we can see that the Hercynian directions of folding vary between north-west in the northern part to north-north-east more in the south; slaty cleavage is either absent or very minimal and localized (more in the south); also the "cleavage front" for this part of the Hercynian fold belt appears only in the region of Goulimine (G. Choubert and Ph. Matte, personal communication), and its extension to the north should reach the fault somewhere west of Agadir. North of the fault, on the other hand, the series show a strong slaty cleavage everywhere, at least to the south of Marrakech, so that the relative shifting of the cleavage front could well be 200 km. A right lateral slip along the fault line would also be consistent with a clockwise rotation of the fold axis in the vicinity of this fault, which can be observed in some places. A detailed study of the striations has not yet given conclusive results about this probable slip direction.

The principal structure discussed above is accompanied by many similar faults, which are smaller and less important. One of them can be observed near Taddert, at the north-eastern end of the Precambrian massive of the High Atlas. In the south-west, all the long straight faults which disappear into the Triassic deposits of the Argana basin, could well be strike-slip faults of the same kind. On the northern side of the High Atlas, J.-P. Schaer also noticed the existence of Hercynian faults^{5,6}. In our opinion, these faults are a general feature of the Hercynian period in Morocco, and should certainly be helpful in understanding this period. For instance one can point out the recent discovery of such wide strike-slip faults in the Moroccan meseta⁸.

Rod⁹ has reported large scale strike-slip faults in the north-west corner of the Sahara shield. For example, he thought that the "South Atlantic fault" ("Agadir fault") could be regarded as a right lateral strike-slip fault. But the principal fault we discussed does not correspond in position with the "Agadir fault", except on its western half. Also, he concluded, just as Dubourdieu¹⁰ did, that these strike-slip faults had been active mainly during the Tertiary period, at the same time as the Canary Islands Volcanoes. Therefore, his hypothesis is very different from ours.

Finally, we note that this Tizi n'Test strike-slip fault should probably extend into the North American block, which was

still contiguous in Hercynian times. One of the "fits" (Fig. 3) proposed shows that the very distinct limit between the Northern and Southern Appalachian mountains (New York region)¹¹ lines up with the trend of the Tizi n'Test strike-slip fault. Thus we feel that the Tizi n'Test strike-slip fault might be of continental importance.

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BIOLOGICAL SCIENCES

Prebiotic Phosphorylation of Thymidine at 65° C in Simulated Desert Conditions

IN many deserts the surface is heated to high temperatures by the Sun each day. In the Sonoran Desert at Yuma, Arizona, for example, the mean surface temperature exceeds 40° C for 10 h and exceeds 50° C for 4 h on an average summer day¹. The highest recorded temperature is 65° C. These temperatures are not extreme; they are typical of fairly large areas of the Earth's surface today. Surface temperatures have been recorded in excess of 75° C in Death Valley, California, on a summer afternoon (W. Fuller and R. Sanchez, unpublished results). The maximum surface temperature recorded on the Earth, outside volcanoes or hot springs, is 82° C².

The same regions that are heated intensely during summer days are subjected to much cooler, damper conditions at other times. In many deserts the surface is moistened with dew at night³. In almost all deserts there is some rainfall during the cooler months. Thus, there are many deserts where the soil is alternately baked dry at temperatures around 65° C and wetted at much lower temperatures. A similar alternation in conditions almost certainly occurs on some sea-shores, but here we have no quantitative data.

We have reported the phosphorylation of nucleosides using mixtures of urea and inorganic phosphate⁴, and have found that monoalkylureas, unsymmetrical dialkylureas or, less effectively, glycnamide can replace urea in this reaction (M. J. B. and L. E. O., unpublished results). Here we give details of the phosphorylation of thymidine in a variety of conditions at 65° C to demonstrate that the reaction could readily take place in deserts nowadays. This, we believe, shows that urea-phosphate mixtures, or closely related mixtures, could

have been important as phosphorylating agents on the primitive Earth.

Reaction products were identified by comparing their chromatographic and electrophoretic mobilities (Table 1) with those of authentic materials, and by enzymatic degradation.

Table 1 R_F Values and Electrophoretic Mobilities

Compound	R_u		R_m III
	I	II	
Uridine	1.00	1.00	—
Uridine 2', (3')-phosphate	—	—	1.00
Thymidine	1.82	1.16	0
Thymidine 3'-phosphate	0.20	0.72	0.94
Thymidine 5'-phosphate			
Thymidine 3',5'-diphosphate	0.03	0.28	1.34

The R_u values are given relative to uridine; and the R_m values relative to uridine 2',3'-phosphate (at 3,000 V for 30 min; migration is towards the anode).

We carried out paper chromatography by the descending technique on Whatman 3MM paper. The solvent systems were mixtures containing the following proportions (by volume): system I, *n*-butanol and 5 M acetic acid (2 : 1); system II, 95% ethanol and 1 M ammonium acetate, made up to 2×10^{-3} M with ethylenediaminetetraacetic acid (EDTA) and adjusted to pH 5.0 with glacial acid (7 : 3). We carried out paper electrophoresis on Whatman 3MM paper at 3,000 V, with 'Varsol' as the coolant. The buffer used was 0.03 M potassium phosphate, pH 7.1 (system III).

We estimated the amounts of radioactively labelled compounds by cutting the paper chromatograms or electrophoretograms into strips and passing these through a scanner with integrator (Baird Atomic RSC 363). The radioactive zones were then cut out and counted more accurately in a Beckman liquid scintillation counter. We calculated the yields by taking the counts in the radioactive zones as a percentage of the total number of counts on the paper, after allowing for background.

Bacterial alkaline phosphatase (220 U ml.⁻¹) (Worthington) was used for the hydrolysis of primary phosphate esters. Incubation mixtures contained 5 absorbance units of substrate, 100 μ l. of a solution which was 0.05 M in Tris-HCl and 0.02 M in MgCl₂ (pH 8.2) and 10 μ l. of enzyme suspension. The incubation period was 2 h at 37° C. Crude rattlesnake venom (from *Crotalus adamanteus*) (Sigma) was used to hydrolyse 5'-linked primary phosphate groups while leaving 3'-linked groups unchanged. A stock solution in 0.1 M Tris-HCl (pH 9.0) containing 10 mg of venom ml.⁻¹ of buffer was prepared. Incubation mixtures contained 5 absorbance units of substrate, 0.1 M Tris-HCl (pH 9.0) (75 μ l.) and the enzyme solution (10 μ l.), and were kept at 37° C for 2 h.

Reaction mixtures were first subjected to chromatography in system II, which separates thymidine T, thymidine monophosphates Tp and pT, and thymidine 3',5'-diphosphate pTp (Table 1). The proportion of 3' and 5'-monophosphates (Tp and pT) in the monophosphate mixture was next determined by degradation with crude rattlesnake venom followed by chromatography in system I. The identity of the Tp was confirmed by degradation to T with bacterial alkaline phosphatase, followed by chromatography in system I. The identity of the diphosphate pTp, obtained in the initial chromatography (system II), was confirmed by electrophoresis in system III, followed by chromatography in system I. The pTp was then eluted and degraded with bacterial alkaline phosphatase. The product (T) was identified by chromatography in system I.

We prepared a solution containing 0.4 M urea, 0.4 M ammonium chloride, 0.04 M thymidine 2-¹⁴C (0.1 mCi/mmol) and 0.04 M Na₂HPO₄. Samples of this solution (0.1 ml.) in borosilicate glass tubes were evaporated to dryness under reduced pressure. The tubes were then placed in an oil bath at 65° $\pm$ 1° C

and a stream of dry nitrogen was passed through them. From time to time tubes were withdrawn and allowed to cool. The contents were then dissolved in water and analysed by chromatography. A precisely similar series of experiments was carried out with the samples freely open to the atmosphere. The results of these experiments are presented in Table 2.

Table 2 Phosphorylation of Thymidine with Na₂HPO₄, NH₄Cl and Urea

Days	T		Tp and pT		pTp	
	(1)	(2)	(1)	(2)	(1)	(2)
1	98.9	—	0.2	—	—	—
3	95.2	97.5	4.2	2.5	0.6	—
9	87.4	95.0	12.5	4.0	1.1	1.0
16	79.8	89.1	17.8	8.2	2.4	2.7

Molar ratio of thymidine, Na₂HPO₄, NH₄Cl and urea, 1 : 1 : 10 : 10, at 65° C in borosilicate glass tubes, (1) at ambient humidity and (2) under a stream of dry nitrogen. Yields given in % of total T present.

The solution described above was also used in experiments designed to measure the extent of reaction during cycles of heating and cooling of the type that might occur in deserts. Reactions were carried out on 1-cm squares of glass fibre paper (Whatman GF 82), with 0.1 ml. of solution on each square. The samples were dried in the air for 18 h and placed at the bottom of individual open test tubes. The tubes were then alternately heated in a block at 65° $\pm$ 1° C for 17 h and allowed to stand at room temperature (25° C) for 7 h; after the first 0.5 h at room temperature 5 μ l. of water was added to each tube. Another set of samples were treated in the same way, except that they were not wetted. The results are presented in Table 3.

Table 3 Phosphorylation of Thymidine with Na₂HPO₄, NH₄Cl and Urea

Days	T		Tp and pT		pTp	
	(1)	(2)	(1)	(2)	(1)	(2)
4	92.6	88.8	7.4	11.2	—	—
9	87.2	77.1	12.8	20.9	—	2.0
13	82.1	62.0	17.9	31.7	—	6.3
18	78.1	54.0	20.0	39.5	1.9	6.5
25	73.2	45.2	22.9	45.3	3.9	9.5

The molar ratio was 1 : 1 : 10 : 10, at 65° C for 17 h each day and at 25° C for 7 h, (1) kept dry and (2) wetted after 0.5 h of cooling to ambient temperature. Yields are given in % of total T present.

The phosphorylation of thymidine by mixtures of urea with phosphate, pyrophosphate, and tripolyphosphate was investigated as follows. We prepared three solutions containing 0.4 M urea, 0.4 M ammonium chloride, 0.04 M 2-¹⁴C-thymidine (0.1 mCi/mmol) and A, 0.12 M Na₂HPO₄, B, 0.06 M Na₄P₂O₇, or C, 0.04 M Na₅P₃O₁₀. The samples were heated continuously at 65° $\pm$ 1° C on glass-fibre paper as described above. The results are presented in Table 4. The samples that had been heated for 44 days all contained Tp and pT in the ratio 27 : 73.

A series of control experiments was carried out omitting (i) urea, (ii) NH₄Cl and (iii) both urea and NH₄Cl. No reaction occurred after 20 days in (ii) or (iii); in (i) a 2.1% yield of thymidine phosphates was formed from solution B and a 3.2% yield from solution C. Preliminary experiments showed that a mixture of urea and trimetaphosphate does not phosphorylate thymidine.

These results confirm that good yields of nucleotides are obtained when nucleosides are heated with urea-phosphate mixtures at 65° C. The reactions proceed somewhat faster at moderate humidities than in a stream of dry nitrogen. Occasional wetting leads to even faster and more extensive reaction. It seems certain that similar reactions would occur in the surface layers of deserts. We hope to demonstrate this directly, when we have developed techniques for maintaining sterile conditions in moist desert sand.

Table 4 Phosphorylation of Thymidine with Various Mixtures heated for 44 Days

Days	T			Tp and pT			pTp	
	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)
1	97.4	91.3	89.4	2.6	8.7	10.6	—	—
2	92.9	84.6	78.0	7.1	15.4	16.8	—	5.2
3	89.9	77.4	73.9	10.1	20.0	20.0	—	2.6
4	86.6	73.4	67.2	12.9	22.4	22.4	0.5	4.2
5	83.9	67.1	61.3	14.8	26.1	25.1	1.3	6.8
7	80.2	59.0	55.8	17.8	31.2	25.9	2.0	9.8
12	73.0	48.1	38.9	23.4	37.5	36.1	3.6	14.4
20	65.3	36.3	24.9	29.3	42.9	41.4	5.4	20.8
22	64.0	36.3	23.4	30.9	44.1	42.4	5.1	19.6
31	59.4	31.2	20.3	34.2	43.6	41.1	6.4	25.2
44	52.2	29.2	18.0	38.8	46.1	38.7	9.0	24.7

(1) Thymidine, Na_2HPO_4 , NH_4Cl and urea, molar ratio 1 : 3 : 10 : 10; (2) thymidine, $\text{Na}_4\text{P}_2\text{O}_7$, NH_4Cl and urea, molar ratio 1 : 1.5 : 10 : 10; and (3) thymidine, $\text{Na}_5\text{P}_3\text{O}_{10}$, NH_4Cl and urea, molar ratio 1 : 1 : 10 : 10 at 65° C. Yields are given in % of total T present.

We have recently demonstrated that inorganic polyphosphates are formed from urea and orthophosphate (L. E. O. and R. Osterberg, in preparation), so it may be significant that mixtures of urea with inorganic polyphosphates are excellent phosphorylating agents. The failure of mixtures of urea and trimetaphosphate to react with nucleosides is surprising.

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Binding of *d*-Lysergic Acid Diethylamide to Subcellular Fractions from Rat Brain

We have examined some of the characteristics of LSD (*d*-lysergic acid diethylamide) binding to subcellular fractions from rat brain, on the assumption that whatever the mode of action of LSD may be, the drug must first bind to LSD receptors. Studies on a model LSD receptor, that is, the receptor site of an antibody to *d*-lysergamide, have already been described¹.

The binding of generally labelled ³H-LSD (1.9 Ci/mmol⁻¹, New England Nuclear) to tissue fractions was studied by suspending 8 mm dialysis bags, containing 0.4 ml. of sample, in a bath of 50 ml. of a modified Krebs Ringer solution (pH 7.25). The bath was flushed with N₂ and contained 0.01% ascorbic acid to reduce oxidation of ³H-LSD. The bath also contained varying concentrations of ³H-LSD and unlabelled LSD, and in some cases other drugs as well^{2,3}. After dialysis of the sample overnight in the dark at 4° C, we measured in triplicate, by liquid scintillation techniques, the radioactivity in equal volumes of bag and bath.

The excess radioactivity in the dialysis bag over that in the bath represents the amount of ³H-LSD taken up at equilibrium by the contents of the bag and it is this excess that is plotted

in the figures. By this measurement, we determined the amount of LSD taken up by synaptosomes, myelin and mitochondria at LSD concentrations ranging from 10⁻¹⁰ M to 10⁻⁴ M in order to detect and characterize various types of LSD binding (Fig. 1).

The known lipid solubility of LSD might be expected to preclude detection of a small population of specific LSD-binding macromolecules. Indeed, equilibrium dialysis of the myelin and mitochondrial fractions showed binding directly proportional to LSD concentration between 10⁻¹⁰ M to 10⁻⁴ M (Fig. 1). This is equivalent to and indistinguishable from a large concentration of non-specific LSD binding sites (dissociation constant = $K_D > 10^{-4}$ M). The synaptosome fraction also showed this type of binding, but at low LSD concentrations there was additional binding which did not occur in myelin or mitochondria (Fig. 1). We have seen these results in five or more preparations of each of the three fractions. The additional specific binding in synaptosomes shows two classes of LSD binding sites, with $K_{D1} = 9.0 \times 10^{-9}$ M and $K_{D2} = 1.2 \times 10^{-6}$ M (Fig. 2). The concentration of the two sites is 6.4 and 340 pmol g⁻¹ fresh weight of tissue, respectively. The concentration of the high affinity sites is thus exceedingly low. We did not detect binding sites of still higher affinity, which limits their concentration to 5×10^{-11} M during dialysis.

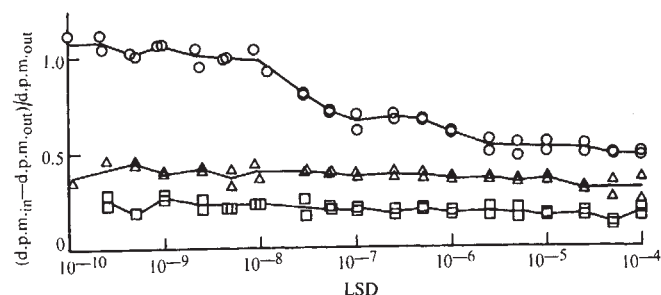


Fig. 1 High affinity LSD binding in synaptosomes and its absence in myelin and mitochondria. The amount of LSD taken up during equilibrium dialysis at various LSD concentrations (10⁻¹⁰ M to 10⁻⁴ M) by constant concentrations of synaptosomes (○), mitochondria (△) and myelin (□) derived from rat cerebral cortical grey matter was determined. At 4.5×10^{-9} M LSD, for example, the bath contained 1,860 d.p.m. 0.10 ml.⁻¹ (d.p.m._{out}) and the synaptosome sample contained 3,690 d.p.m. 0.10 ml.⁻¹ (d.p.m._{in}); d.p.m._{in} - d.p.m._{out}, the difference between the radioactivity in the dialysis bag and the radioactivity in the bath after dialysis (1,830 d.p.m. 0.10 ml.⁻¹ in this case), represents the amount of ³H-LSD taken up by the tissue. This amount multiplied by $[\text{LSD}]_{\text{total}}/[\text{LSD}]$ represents total LSD taken up. If the ratio (d.p.m._{in} - d.p.m._{out}) / d.p.m._{out} is greater at a low LSD concentration than at higher LSD concentrations, high affinity binding is present. Myelin and mitochondria lack the high affinity binding sites present in synaptosomes. Subcellular fractions were prepared from rat brain cerebral cortical grey matter of 190–250 g Sprague-Dawley rats by a slight modification⁴ of Gray and Whittaker's procedure⁵. The crude mitochondrial fraction in 0.32 M sucrose was layered on top of a discontinuous sucrose gradient (1.2 and 0.8 M sucrose) and centrifuged at 200,000g for 75 min in a Spinco SW-50 rotor to yield myelin, synaptosomes and mitochondria. The myelin and synaptosome fractions were diluted with water to 0.32 M sucrose and centrifuged at 200,000g for 45 min. The pellets, and the mitochondrial pellet, were suspended in the buffer mentioned. The purity of the ³H-LSD was periodically checked by thin-layer chromatography on Eastman silica gel sheets. If more than 5–10% of the ³H-LSD was degraded it was repurified by the same method. The solvent system was CHCl_3 : ethanol : acetic acid (105 : 15 : 1.5) containing 0.01% ascorbic acid. The chromatograms were prepared and run in an N₂ atmosphere in the dark at 4° C. The myelin and mitochondria results plotted in this figure are each from four experiments and the synaptosome results are from two experiments. Protein concentrations are: myelin, 2.6 mg ml.⁻¹; mitochondria, 4.6 mg ml.⁻¹; synaptosomes, 11.4 mg/ml. Nitrogen concentrations are: myelin, 0.42 mg ml.⁻¹; mitochondria, 0.76 mg ml.⁻¹; synaptosomes, 1.38 mg ml.⁻¹. The protein content was determined by the method of Lowry *et al.*⁶, using human serum albumin as a standard, and nitrogen content was determined by the method of Lang⁷.

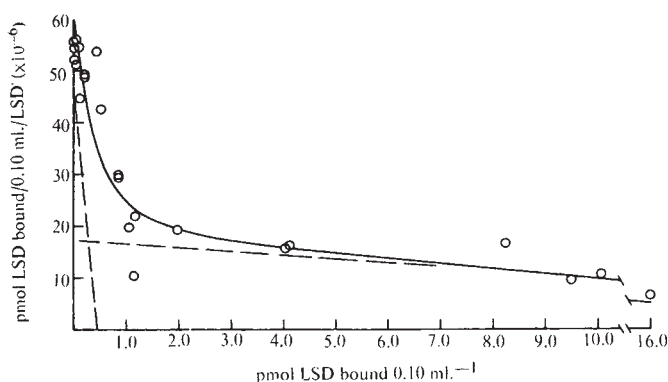


Fig. 2 The amount of LSD taken up by synaptosomes during equilibrium dialysis is expressed as a Scatchard plot⁸ in order to determine the number, affinity, and concentration of high affinity binding sites. The points are experimental data. The curve is a theoretical curve for binding by two classes of binding sites with dissociation constants of 9.0×10^{-9} M and 1.2×10^{-6} M and present at concentrations of 0.40 pmol 0.10 ml.⁻¹ (6.4 pmol g⁻¹ fresh weight of tissue) and 21 pmol 0.10 ml.⁻¹ (340 pmol g⁻¹ fresh weight of tissue), respectively. The dashed lines indicate the two classes of binding sites.

We chromatographed a portion of the bath contents from myelin, synaptosomes and mitochondria dialysed against 10^{-6} M ³H-LSD and found that 10–15% of the ³H-LSD was degraded, but the degradation product did not exhibit high affinity binding to synaptosomes. ³H-LSD was probably not metabolized to some chromatographically similar compound because brain tissue does not metabolize LSD⁹.

We measured the inhibition by various compounds (all at 10^{-6} M) of 5.4×10^{-9} M ³H-LSD binding to synaptosomes (Table 1). At 5.4×10^{-9} M, ³H-LSD binds to both the high affinity site and the lower affinity site, in the ratio of 1.6 : 1. Among the synaptic transmitter candidates and their meta-

Table 1 Inhibition of the ³H-LSD Binding to Synaptosomes by Various Compounds

Inhibitor	Inhibition (%)	Inhibitor	Inhibition (%)
Transmitters and metabolites		Amino-acids	
Serotonin	70	L-Tryptophan	3
5-Hydroxyindole acetic acid	—7	L-Phenylalanine	0
Tryptamine	40	L-Tyrosine	5
Melatonin	14	L-Glutamate	16
L-Epinephrine	5	Others	
L-Norepinephrine	23	Ergonovine	70
DL-DOPA	—6	Tyramine	5
γ-Aminobutyric acid	2	d-Amphetamine	5
Hallucinogens		Morphine	—2
Mescaline	1	Spermidine	18
2,5-Dimethoxy-4-methyl-amphetamine (DOM)	25	Adrenochrome	34
Psilocybin	5	Histamine	—3
Psilocin	56		
5-Methoxytryptamine	55		
5-Methoxy-N,N-dimethyl-tryptamine	46		
N,N-Dimethyltryptamine (DMT)	27		
Bufotenine	52		
Harmaline	28		

In all cases the LSD was 5.4×10^{-9} M, all as ³H-LSD, and the inhibitor concentration was 10^{-6} M. Both LSD and inhibitor were added simultaneously to the bath at the beginning of the experiment. For 100% inhibition, we used 10^{-4} M unlabelled LSD as inhibitor. Thus we measured only inhibition of specific LSD binding without interference by lipid/buffer partitioning or non-specific binding of LSD. The sources of the drugs and the preparation of psilocin from psilocybin have been previously described⁴. Data are mean values from two or three different synaptosome preparations. Mean values were all within 5% inhibition, except for the following: serotonin, ergonovine, amphetamine, $\pm 12\%$; DOPA, DOM, tryptophan, $\pm 20\%$; 5-hydroxyindole acetic acid, tyrosine, $\pm 25\%$.

bolites, serotonin, norepinephrine and tryptamine were inhibitory. LSD may interact with serotonin¹⁰ or norepinephrine receptors¹¹. Marchbanks reported 50% inhibition by 4×10^{-7} M LSD of ³H-serotonin binding to synaptosomes (K_D for serotonin = 5×10^{-7} M)¹². Glutamate inhibited slightly, and the other three amino-acids tested were ineffective. Glutamate may function as a transmitter substance in the mammalian central nervous system^{4,13}. Ergonovine, a lysergamide derivative, was a potent inhibitor.

All of the hallucinogenic compounds we tested were inhibitory at 10^{-6} M except for mescaline and psilocybin. Mescaline at 10^{-4} M, however, inhibited 50% of the LSD binding. Psilocybin is probably not hallucinogenic but is rapidly dephosphorylated in the body¹⁴ to the potent hallucinogen psilocin. Psilocybin did not compete for LSD binding, but psilocin did.

In spite of considerable differences in their structures, mescaline, psilocin and LSD show cross tolerance and produce symptoms similar in many respects, suggesting that their behavioural effects may be mediated at the same sites in the central nervous system, perhaps at a common set of post-synaptic receptors^{15–17}. The potencies of these compounds in man are very different, however, for a variety of possible reasons (metabolism, passage across the blood-brain barrier, and so on). The ratio of potencies in man is 1 : 32 : 4,500–9,275 (mescaline : psilocin : LSD)^{17,18}. Mescaline at 10^{-4} M and psilocin at 10^{-6} M inhibited 5.4×10^{-9} M LSD binding to synaptosomes by 50%, so the ratio of inhibitory potency is 0.32 : 32 : 6,400 (mescaline : psilocin : LSD). The strong similarity between the ratios for hallucinogenic potency and inhibitory potency implies that these three drugs act at the same synaptic sites.

Diab, Freedman and Roth have recently observed in autoradiographs ³H-LSD of high specific activity bound to neurones of rat brain cortex¹⁹. Our results are complementary to and consistent with their observations on cerebral cortical tissue.

It is not possible to know which of the two LSD binding sites is related to the hallucinogenic properties of the drug, or whether both sites are involved, but the extremely low effective dosage of LSD leads us to favour the higher affinity site.

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Liver Zinc in Carcinoma

IN contrast to the important role of zinc in wound healing^{1,2} comparatively little attention has been paid to the metal in relation to tissue reaction to malignant disease³⁻⁸. In this study samples of liver tissue from fifty necropsies were divided into four series (excluding malignant tissue itself): "normal" liver (series I), fatty liver (series II), apparently uninvaded liver from organs containing secondary malignant deposits (series III) and livers from patients with malignant disease but no obvious liver secondaries (series IV). The selection, preliminary processing and preparation of the specimens will be described elsewhere⁹. All specimens were analysed in duplicate. One set of samples was wet-digested and used for the measurement of

Table 2 Two Examples of the Zinc-concentration Gradient in Livers containing Malignant Deposits

	Ash zinc (p.p.m.)	
	Liver A	Liver B
Necrotic core of tumour	4,000	2,850
Periphery of tumour	5,000	3,850
Apparently normal tissue adjacent to tumour	11,800	
Apparently normal tissue remote from tumour	12,300	7,900

pretations. A "pre-malignant state" associated with a considerable accumulation of zinc in the tissues might be widespread in patients who die from the disease. More probably, the increase in liver zinc could reflect a defence reaction to invasion by malignant cells. This could apply even to organs which contained no naked-eye deposits. (A link may exist between the role of zinc in wound healing and the accumulation of zinc in tissues reacting to malignant disease.) Last, it is conceivable though unlikely that the rise in liver zinc might be associated with the poor nutritional state common in the terminal stage of cancer rather than with the cancer itself. (The relation between general nutritional state and zinc is still unclear; but, on circumstantial evidence^{2,16}, in malignant cachexia one might expect a decrease rather than an increase in tissue zinc.) The striking accumulation of an easily measurable trace metal in the liver in malignant disease might be of diagnostic use in the interpretation of liver-biopsy material.

Table 1 Comparative Results of Zinc Concentrations in Five Types of Liver Tissue

Type of sample	"Normal" (series I)	Fatty liver † (series II)	Secondaries in liver * (series III)	Malignancy outside liver (series IV)	Malignant tissue
No. of samples	18	13	10	9	8
Mean ash zinc (p.p.m.)	5,880	7,320	9,690	8,570	3,300
s.d.	1,670	2,220	2,160	2,140	570
P (in relation to series I)	—	<0.005	<0.0005	<0.0005	<0.0005

* All samples were removed from uninvaded areas which showed no naked-eye or microscopic evidence of malignancy.

† Liver fat estimated by method based on ref. 10.

zinc concentration by atomic-absorption spectroscopy. The other set of samples was ashed and used for the determination of the wet-weight/ash ratio. Closely adjacent specimens were examined microscopically to exclude histological evidence of local malignant invasion. Zinc concentrations were finally expressed in terms of ash weight tissue. (In this context this is a more meaningful reference datum than "dry" weight, wet weight or protein or nitrogen concentration.) The results are summarized in Table 1. "Normal" liver (series I) refers to organs which had been removed from subjects who showed no evidence of malignant disease anywhere, and whose liver showed only mild terminal changes. The range of zinc concentrations in this series was comparatively narrow and is in fairly close agreement with the findings of other workers^{3,11-15}. The difference between normal liver zinc and liver zinc from subjects with malignant disease (series III and IV) was highly significant ($P < 0.005$ and $P < 0.0025$ respectively). The difference between the two malignant-disease series was insignificant compared to the difference between the two malignant-disease series combined on the one hand and the two non-malignant series combined on the other.

Carcinomatous deposits themselves had a low zinc concentration both in terms of mean concentration and of range of values (mean: 3,300 p.p.m.; range: 250-4,440 p.p.m.). Because of this and because of the abnormally high zinc content of organs harbouring such deposits there was a steep zinc-concentration gradient when samples were analysed moving from the necrotic core of a secondary growth to the apparently uninvaded surrounding tissue (Table 2).

The high zinc concentration in apparently unaffected liver tissue from subjects with carcinoma is open to several inter-

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Presence of Egg Antigen in Immature Oocytes and Preimplantation Embryos

THE availability of a species-specific antibody against mouse eggs which did not react with mouse somatic cells^{1,2} has made it possible to determine the presence of the "egg antigen" in both oocytes and developing embryos. Oocytes were obtained from Swiss albino ICR mice either by disruption of intact ovaries with thin needles (4 to 6-day-old mice) or by disruption of follicles (older mice). Unfertilized eggs were obtained from superovulated Swiss mice as before³. Embryos at different stages of development were flushed from oviducts and uteri of untreated Swiss mice at various times after mating. The day on which the vaginal plug became visible was counted as the first day of pregnancy. Postimplantation embryos were dissected by Kirby's⁴ technique and cumuli oophori and zonae pellucidae were removed by the standard procedure³. Trophoblast cultures were established from late blastocysts maintained in the wells of microtest tissue culture plates for 48 h in Eagle's minimum essential medium supplemented with 10% foetal bovine serum. Trophoblast giant cells were obtained from ectoplacental cones of 7.5-day-old embryos which had been treated for 15 min with a 0.25% trypsin solution, containing 200 µg of DNAase/ml. to remove adhering fibrinoid deposits⁵.

For the production of antibody, a female guinea-pig was injected subcutaneously five times with 150–250 unfertilized eggs, without zonae pellucidae, in complete Freund's adjuvant. The cells had been treated with pronase and rinsed repeatedly in Whitten and Biggers medium and in balanced salt solution. Serum obtained from the guinea-pig 20 days after the beginning of immunization and 2 days after the last injection, lysed unfertilized mouse eggs without zonae pellucidae throughout a 1:200 dilution. When the immunized guinea-pig received two booster injections of eggs 6 weeks after the first series of immunizations, the cytotoxic titre of its serum increased to 1:6,400. Both anti-egg (AE) sera were used in the cytotoxic tests (Tables 1 and 2).

Table 1 Influence of Anti-egg (AE) Serum on Mouse Oocytes

Source and treatment of oocytes	Relation of cells destroyed after exposure to serum dilutions					
	Control serum 1:10	AE serum 1 (titre 1:200) 1:10	AE serum 1 (titre 1:200) 1:100	AE serum 2 (titre 1:6,400) 1:10	AE serum 2 (titre 1:6,400) 1:100	AE serum 2 (titre 1:6,400) 1:1,000
Oocytes of <20 µm diameter from 4 to 6-day-old mice*	0/94	0/88		20/20	23/23	0/26
Larger oocytes from immature follicles of 2 to 3-week-old mice†	0/20	25/25	25/25			
Mature oocytes from disrupted follicles of 6-week-old mice†	0/29	20/22	10/10			
The same as above with zonae pellucidae	0/10‡			10/10‡	10/10‡	0/10‡
Unfertilized eggs with zonae pellucidae	0/10‡			10/10‡	0/10‡	

* These oocytes have no zonae pellucidae which could be identified at light microscopy level.

† After removal of zonae pellucidae.

‡ Verified by fluorescein diacetate staining⁷.

Cytotoxic tests were carried out on unfertilized eggs and embryonic material as before¹. Preimmunization serum, or serum obtained from guinea-pigs injected only with adjuvants, was used as control serum in each test. The reactivity of the AE serum for lymphocytes and cumulus oophorus cells was

determined by a slight modification of Bodmer's⁶ technique. The results (Table 1) indicate that egg antigen could already be detected in oocytes of less than 20 µm diameter, if a high-titre AE serum was used. The larger oocytes were lysed even by the low-titre serum. The presence of zonae pellucidae did not prevent, but greatly reduced, immune lysis of the cells.

Table 2 Influence of Anti-egg (AE) Serum In Pre- and Postimplantation Mouse Embryos

Embryos	Stage of development	Ratio of embryos destroyed after exposure to serum dilutions			
		Control serum 1:10	AE serum 1 (titre 1:200) 1:10	AE serum 1 (titre 1:200) 1:100	AE serum 2 (titre 1:6,400) 1:10
Preimplantation	2-celled	0/30	20/20	17/20	
	4 to 10-celled morulae	0/10	10/10	10/10	
		0/13	13/13	17/17	
	Early blastocysts				
	External part	1/17	25/25	22/22	
	Inner cell mass	1/17	22/25	12/22	
	Late blastocysts				
	External part	0/21	23/23	11/22	39/39
Postimplantation	Inner cell mass	0/21	0/23	0/22	19/39*†
	Inner cell masses‡	0/13	0/13		
	6 to 7-day-old egg cylinders	0/15	0/8*		0/7
	The same treated with 0.25% trypsin and 0.1% DNAase for 15 min	0/9	0/9*		
	Trophoblast cultures	0/6			0/6
	Trophoblast giant cells				No cytotoxic effect

* Verified by fluorescein diacetate staining⁷.

† Destroyed after additional 30 min incubation.

‡ To obtain inner cell masses late blastocysts were incubated in AE serum for 30 min, damaged external cells were removed with 0.5% pronase and 0.2 DNAase, and the inner cell masses re-exposed to the AE serum.

As Table 2 shows, the egg antigen could be detected in embryos throughout the late blastocyst stage, the inner cell mass of the blastocyst being slightly less susceptible to immune lysis than the external part. No cytotoxic reaction was observed when 6 to 7-day-old egg cylinders or trophoblast giant cells were exposed to the serum. AE serum at 1:10 concentration had no lytic effect on lymphocytes, red blood cells or cumulus oophorus cells of Swiss mice. Spermatocytes obtained from minced testes of Swiss mice were also resistant to lysis. Intraperitoneal injection of 0.35 ml. of high-titre AE serum into 3-week-old Swiss mice did not evoke perceptible changes in the ovaries.

These results indicate that egg antigen is present on small oocytes, eggs and preimplantation embryos throughout the late blastula stage. During maturation the immunosensitivity of oocytes to AE antibody increases, for higher concentrations of anti-egg antibody were needed to lyse small oocytes than more mature oocytes. This may be caused by an increased concentration of egg antigen on the surface of mature oocytes. Since the synthesis of proteins almost stops in unfertilized eggs^{8,9}, it is doubtful whether at that time the egg antigen is still being synthesized. It is also impossible at present to ascertain whether synthesis of egg antigen still occurs after fertilization or whether the presence of the antigen on the surface of preimplantation embryos is the result of its accumulation during maturation of the oocytes. Decreased immunosensitivity of late blastocysts, particularly inner cell masses, to the anti-egg antibody may indicate a gradual

depletion of the accumulated antigen. Conversely, it is possible that egg antigen is synthesized during the entire pre-implantation period. The egg antigen could not be detected by the immunosensitivity test in postimplantation embryos. Its repression in somatic cells and spermatocytes seems to last during the lifetime of the animal. But because it seems to be impossible to immunize Swiss mice against Swiss egg antigen (unpublished data), the small amount of antigen needed to evoke tolerance may be present in the animal host.

The fact that guinea-pig serum produced against mouse somatic cells transformed by simian virus 40 is cytotoxic for mouse eggs² indicates that the mechanism for egg antigen synthesis may be activated in somatic cells of adult animals.

The relationship, if any, of the egg antigen to H-3 and H-6 histocompatibility antigens which were found on preimplantation embryos^{10,11} merits investigation for elucidation of its role in the immunology of early pregnancy.

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Induction of Chronic Polyarthritis in Rabbits

THE aetiology and pathogenesis of rheumatoid arthritis remain obscure¹, and progress is hindered by the unavailability of a suitable animal model for laboratory studies. Attempts to produce experimental arthritis resembling rheumatoid arthritis have used chiefly infectious agents or immunological responses². None of these forms of animal arthritis, however, is quite equivalent to that of human disease.

We observed, while studying pyelonephritis^{3,4}, that one of the rabbits immunized with heat-killed *Escherichia coli* O:14 developed arthritis. For studying the pathogenesis of rheumatoid arthritis from a standpoint of infection and immunity, we have analysed this experimental approach of polyarthritis further and find that it has a close resemblance to the disease.

Heat-killed *E. coli* O:14, the O antigen located in the endotoxin moiety (the LD₅₀ of this antigen was 180 µg for mice) contains a common enterobacterial antigen^{5,6} and was used in our experiments. For immunization, twenty rabbits were intramuscularly injected at monthly intervals with 2 ml. of heat-killed *E. coli* O:14 (960 µg) suspended in Freund's incomplete adjuvant into multiple sites of the back. In addition, ten rabbits were similarly injected only with Freund's incomplete adjuvant to serve as controls.

About 10 months after initial immunization, this continuous hyperimmunization with enterobacterial antigens produced polyarthritis in two rabbits. No case of polyarthritis was found in the control group.

In the histopathological examinations of the affected rabbits, various stages of arthritis were seen. Generally, the synovial membrane was thickened, oedematous and infiltrated with lymphocytes and plasma cells, which occasionally formed compact foci resembling the lymph node in the subsynovial tissue. There was much proliferation of the cells covering the hypertrophied synovial villi, deposition of compact fibrin within the synovial membranes, and fibrinoid degeneration in the synovial tissues. The articular cartilage was replaced by fibrous pannus which was seen extending across the joint surface and occasionally destroyed the bony end-plate (Fig. 1).

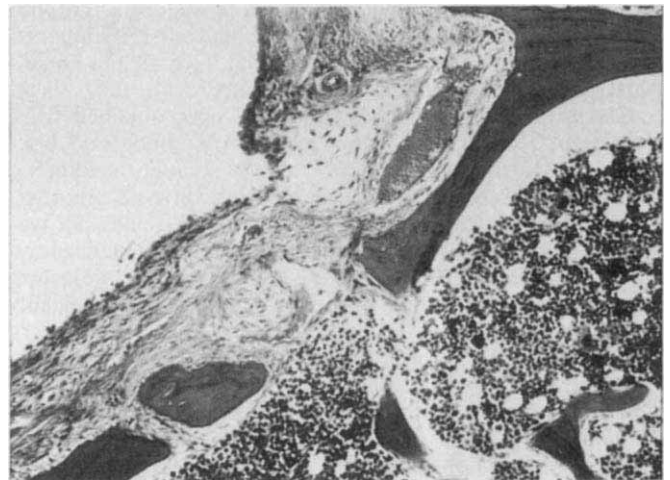


Fig. 1 The shoulder joint showing the fibrous replacement of the articular cartilage and occasional destruction of the bony end-plate. (Haematoxylin and eosin, $\times 75$.)

In some of the affected joints, fibrous tissue filled the joint space and fibrous ankylosis was found. On the other hand, the bacterial cultures from the synovial fluid were negative in the arthritic rabbits at the time of necropsy.

A serum factor (rheumatoid factor like substance, RFLS)⁷ analogous to the human rheumatoid factor has also been induced in the hyperimmunized rabbits. The RFLS was observed primarily with tanned sheep cells coated with aggregated rabbit γ -globulin (Ag.RGG) and demonstrated cross-reactivity with aggregated human γ -globulin (Ag.HGG).

Absorption of the sera with isologous immune precipitate (ovalbumin, anti-ovalbumin) resulted in a marked reduction of the RFLS titres but no change in the *E. coli* agglutinin titres. In density gradient centrifugation studies, the RFLS was contained in the bottom fraction associated with macroglobulin. Furthermore, it was demonstrated that the RFLS was present in the fraction of 19S γ -globulin by gel filtration chromatography with 'Sephadex G-200'.

Immunofluorescent examination of the arthritic rabbits detected the RFLS of the synovial tissues chiefly in the cytoplasm of plasma cells (Fig. 2) and mononuclear cells, occasionally in free state by staining with fluorescent Ag.RGG and rhodamine-labelled Ag.HGG. Rabbit IgM was also present in a similar area. Rabbit IgG was primarily observed in the synovial membranes. Furthermore, the mixed staining using fluorescein and rhodamine conjugates revealed the localization of the β_1c (C'3) component of complement in association with IgG (IgG- β_1c complex).

IgG-RFLS complex was also seen in the synovial tissues. Moreover, small amounts of the sensitizing antigens were found in the synovial membranes.

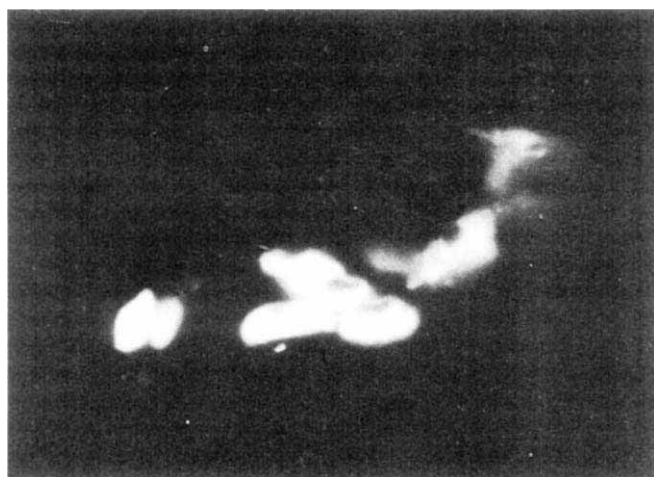


Fig. 2 The immunofluorescent localization of the RFLS within the cytoplasm of plasma cells in the synovium from the affected knee joint. (Staining with fluorescent Ag.RGG, $\times 750$.)

The fact that arthritic rabbits had histopathological features which are considered to be characteristic of human rheumatoid arthritis⁸, such as proliferation of superficial synovial cells, marked infiltration with lymphocytes and plasma cells, the formation of lymphoid nodules, characteristic cartilage destruction and progressive nature of the pathological lesions in spite of negative culture, is of considerable interest. The presence of the RFLS in the sera and immunofluorescent evidence in the arthritic rabbits being similar to immunopathological changes^{9,10} of human RA show that the present animal model is quite analogous to rheumatoid arthritis. The cause of this unusual process is not clear. However, studies on autoimmune mechanism due to modified synovial tissue antigens with endotoxic substance are in progress in view of the present immunological data.

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Impurities in Preparations of *Acetabularia* Chloroplasts

In a recent description of photosynthesis by preparations of *Acetabularia mediterranea* chloroplasts in an artificial leaf¹, it was suggested that the stability and impermeability of these chloroplasts are due to qualities of the chloroplast membrane.

Recent work in this laboratory (F. Winkenbach and R. G. S. Bidwell, in preparation for publication) suggests that these chloroplasts, together with the small quantities of cytoplasm previously noted^{2,3}, are enveloped in the form of droplets by a membrane-like structure. It is therefore possible that the stability and impermeability of *Acetabularia* chloroplasts are due to the presence of this membrane. Varying the proportion of contamination does not appreciably alter the distribution of ¹⁴C among products of photosynthesis, so that it seems unlikely that the cytoplasmic contamination is directly involved in the observed photosynthetic metabolism.

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Promotion of Seed Germination by Nitrates and Cyanides

MANY viable seeds fail to germinate in darkness after imbibing water, but do so to varying degrees in solutions of several compounds. Well known promoters of germination are nitrate, nitrite and various sulphhydryl and gibberellin salts¹. Hydroxylammonium salts, although often cited as inhibitory¹, are known to promote germination at low concentrations². The essential action of none of these is understood and the use of nitrates in seed testing remains empirical. In seeking underlying causes for the promotive effects of nitrates we examined the germination responses to other nitrogenous salts as well as compounds affecting respiration. Cyanides were found to promote germination of many kinds of seeds in extension of the observations of Roberts³.

Seeds of pigweed (*Amaranthus albus* L.) and lettuce (*Lactuca sativa* L. cultivar Grand Rapids) were selected from about fifty species, many of which responded similarly to the several compounds. Duplicate lots of 100 seeds in replicated experiments were placed in covered Petri dishes on filter papers moistened with the appropriate solutions, which were near pH 6 except for cyanides with a pH > 8. The seeds were held in darkness at 25° C for lettuce and 30° C for *A. albus* for 3 days at high humidity before counting of germination. Observations were restricted to salts with ions of as small diameters as possible in order to avoid questions of entry into the seed. Entry was evidenced by aspects of growth after germination. Effects of counter-ions, which were generally Cl⁻, Na⁺ or K⁺, were tested over wide concentration ranges with appropriate salts and found to be negligible.

Nitrate utilized in plant growth is reduced through nitrite, hyponitrite (uncertain), and hydroxylammonium intermediates to the ammonium ion, which is assimilated into amino-acids⁴. Ammonium salts, with but rare exception, have only a small promotive effect on seed germination as is true for *A. albus* (Fig. 1) and lettuce. Accordingly, the action of nitrates depends on one or more of the intermediates or on the reduction process itself, for example, as an alternative oxidant to oxygen as postulated by Roberts³ from observations on barley and rice. Nitrate action is probably mediated by nitrate and nitrite reductases, which are present in many plant tissues⁴. We could not detect such activity, however, until germination occurred. The level of nitrate reductase, though necessarily

adequate for reduction of some nitrate, must be quite low over the periods of our tests. The germination induced, moreover, does not depend on induction of the enzyme, as shown by unchanged germination response in the presence of sodium tungstate⁵ as an inhibitor of induction.

Sodium nitrate and nitrite are similarly effective on germination of *A. albus* seeds with maximal promotion near 10 mM (Fig. 1). Hydroxylammonium chloride is maximally effective at 0.1 mM as also are the N-diethyl and *o*- and N-monomethyl derivatives, as well as 1,1-dimethyl, 1,2-dimethyl, and the unsubstituted hydrazinium salts. These responses and the concentrations needed for action are consistent with the hydroxylammonium ion being the effective intermediate in stimulation of seed germination by nitrate and nitrites. Responses to the alkyl derivatives indicate that the action is not determined by oxime or hydroxamate formations which are blocked by substitution on the nitrogen atom. Hydroxylammonium salts can form complexes with transition group elements and are known to couple as reductants to the respiratory chain at the flavin level with $E' = 0.066$ V for oxidation to nitrite⁶. They inhibit electron transfer to oxygen through cytochromes *b*, *c*, and *a*₃ at high concentrations. A stoichiometric gain of total reductant, of course, is not possible in nitrate reduction.

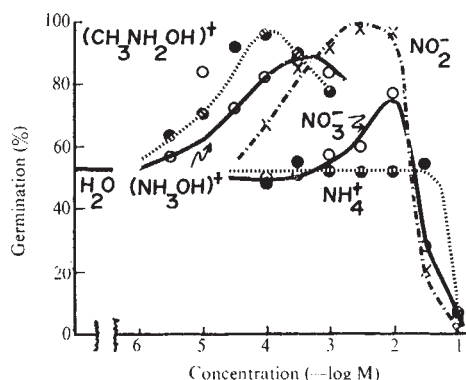


Fig. 1 Effects of sodium nitrate and nitrite and several hydroxylammonium and ammonium chlorides on germination of *Amaranthus albus* seeds.

Because of the likely coupling of hydroxylammonium ions to the respiratory chain and in view of observations³ that cyanide can promote seed germination we were led to measure effects of cyanides, azides, and hydroxamates. Cyanides and azides are widely used as alternative inhibitors of respiration. They are considered to be effective by combination with cytochrome *a*₃ at concentrations below 1 mM. Potassium cyanide solutions promote germination strongly between 0.003 and 3.0 mM with maximal effectiveness near 0.1 mM (Fig. 2). Potassium azide solutions in contrast inhibit germination with half maximal effectiveness near 0.03 mM (Fig. 2). Azides also have a small promotive effect approaching that for cyanides in the range of 0.003 to 0.01 mM. These results indicate that blocking electron transfer to oxygen through the cytochrome chain promotes germination. Both azide and cyanide become inhibitory by other actions at adequately high concentrations.

The blocking action of cyanide on electron transfer to oxygen through cytochromes with the concomitant promotion of seed germination suggests that the latter involves a cyanide-resistant respiratory activity. Bendall and Bonner⁷ have found evidence that a non-haem iron protein is involved in this cyanide-resistant system, which also probably contains a flavin. This system in isolated mung bean and skunk cabbage mitochondria is inhibited by aryl hydroxamates and, to a lesser extent, by thiocyanates⁸, both of which chelate ferric ions. We find that germination of lettuce seeds is 50% inhibited by 20

mM NaSCN. *A. albus* seeds are 50% inhibited by sodium benzohydroxamate at 0.3 mM, which is to be compared with values of 0.4 mM for skunk cabbage and 0.09 mM for mung bean mitochondria⁶. Seed germination is also inhibited by sodium acetohydroxamate with half maximal effect at 3 mM.

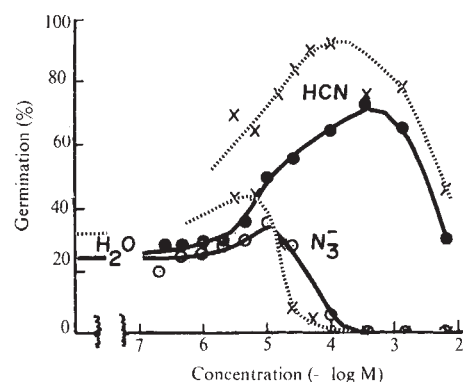


Fig. 2 Effects of potassium cyanide (giving HCN by hydrolysis) and azide on germination of *Amaranthus albus* (---) and *Lactuca sativa* (—) seed germination.

A. albus seed germination is about 75% inhibited by combined use of 1, 0.1, or 0.01 mM KCN with 1.0 mM benzohydroxamate or 0.03 KN_3 . These percentage inhibitions are comparable with values shown by the unpromoted seeds in the absence of cyanide. Assessment of all the effects indicates that both hydroxamates and azides inhibit the system involved in promotion of germination that is activated by cyanide, which is ostensibly the cyanide-resistant respiratory activity studied by Bendall and Bonner⁷.

Potassium oxalohydroxamate, $\text{K}_2(\text{CONHO})_2$, adjacent carbonyl groups of which modify its reactivity and chelation properties relative to monohydroxamates, inhibits germination of *A. albus* seeds by about 50% at 10 mM, but is markedly promotive at 1 and 3 mM. This promotive activity is comparable with that of the hydroxylammonium salts. Both potassium ferrocyanide, as an electron donor, and the ferricyanide, as an electron acceptor, fully promote *A. albus* seed germination at 10 mM. The value of $E'_0 = 0.34$ V indicates coupling with electron transfer between cytochromes *c* and *a* in the fully organized cyanide-sensitive respiratory chain. The ferrocyanides and ferricyanides are unlikely to act other than in an oxidation-reduction capacity. Seemingly enhancement of electron transfer *per se* can also enhance germination irrespective of electron transfer to oxygen through to a cyanide-resistant system.

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Factors influencing Copper Tolerance in *Becium homblei*

THE copper tolerant plant species *Becium homblei* translocates excess copper absorbed during the growing season to the leafy shoots, where it is stored in the cell walls, and the leaves are regularly burnt off in bush fires during the dry season. This has been suggested as an important factor in the evolution of this species¹.

Fire, however, cannot be considered the only extrinsic factor influencing the copper tolerance of this species. Previous work on the ecology of *Becium homblei*^{2,3} has shown that this species is found in a range of soil types, from granite sandveld where metals are in trace quantities, to soils with not only high copper concentrations but also with high levels of nickel, lead and arsenic. The explanation for this diverse tolerance, together with the peculiar distribution of this species in Central Africa^{3,4}, can at present only be given in terms of biotype depletion³⁻⁵. This involves postulating the existence of a widespread, genetically heterogeneous ancestor to the present more isolated populations of *B. homblei*, which was adapted to the prevailing climate over a large part of South Central Africa.

Although it has been shown that the climate of this region varied considerably in the past⁶⁻⁸, seasonal fluctuations between wet and dry periods have been characteristic since the upper Triassic⁸. As a result, many small perennial species such as *B. homblei* which inhabit this area are geophytes. These have large underground rootstocks from which new leafy shoots arise each wet (growing) season and die off during the dry season. With this habit it is hardly surprising that this type of plant is able to survive and even spread into areas which are regularly burnt, such as the derived savanna woodlands^{1,6,9} and even fire maintained montane grasslands in Central Africa¹⁰. This is because the perennating buds are protected below the soil surface during the time of year that natural and man-made fires are prevalent.

It is the effects of climate which cause the annual dying off of aerial shoots of *B. homblei* and this would occur even in the absence of fire. Seasonal fluctuations between wet and dry periods should be considered a fundamental extrinsic factor which acts with the internal mechanisms to produce copper tolerance in this species. *B. homblei* can exist in a variety of soil types, but is confined to fairly well defined climatic boundaries², so it is suggested that only a marked change in climate would result in the disappearance of this species, not prolonged protection from fire.

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Predictions from Play

IN a series of studies of curiosity and exploration in young children¹⁻⁶, it was found that 3 to 5 year olds could be placed in one of three categories, according to their responses to a

new toy. Usually, when a child is confronted with a new toy, he first inspects and investigates it; then, when he is familiar with it, he "plays" with it. These two categories of behaviour have been more formally characterized as "specific" and "diversive exploration" respectively⁷, and their distinctive behavioural features have been described^{4,5}. Essentially, in specific exploration or investigation the implicit query seems to be "What can this object do?"; in diversive exploration or play it is "What can I do with this object?"

The three mutually exclusive categories into which nursery school children fell were as follows: non-explorers (NE) who looked at the new toy and even approached it but did not inspect or investigate it; explorers (E) who actively investigated the toy but thereafter did very little else with it; inventive explorers (IE) who, after investigating the toy, used it in many imaginative ways⁵. Girls were over-represented in the first category, and boys in the third. This finding has been discussed in relation to differences in maturity and aptitudes between the sexes⁸.

But, more specifically, we wished to know if these early individual differences observed in patterns of exploration and play were characteristic and enduring ones, or whether they were simply a function of the experimental situation. In other words, were these behavioural differences predictive of any subsequent tendencies and abilities? The failure to explore, for instance, could be due to a lack of curiosity generally, or in that particular toy, or it could be due to a personality trait such as inhibition, shyness, etc. Again, the differences in inventive play could be due to more active and vigorous play, or they might be the precursors of differences in convergent and divergent thinking, usually referred to as creativity.

It has been possible to re-examine forty-eight children (twenty-three boys, twenty-five girls) of the original sample of almost 100. These children are now at primary school and aged between 7 and 10 years. They were administered the Wallach and Kogan battery of creativity tests⁹ which have been shown to be reliable and valid¹⁰. Two measures can be obtained from these tests: fluency, the total number of responses given to the items; and originality, the number of unique responses given by an individual. Although there is some correlation between the two measures, the performances of boys and girls were not found to be comparable on both measures¹¹, hence only the originality scores, duly weighted¹², are considered here. The children also answered a personality questionnaire especially designed for this age group¹³, and were rated by teachers and parents on a number of personality traits and behavioural characteristics. Details of these procedures will be available elsewhere⁶.

The numbers in the three categories in the earlier study and in the present study are shown in Table 1. Should there be an association between inventiveness in play and creativity in ideas, children in the IE group would be expected to score higher on the Wallach-Kogan tests than those in the E or NE groups. The means and standard deviations (in parentheses) are given in Table 1 as well as the significance of the differences between the means. These results indicated that failure to explore novelty was not necessarily associated with convergent thinking in girls, and that inventive play was positively associated with the propensity for divergent and creative thinking, but particularly so in boys. This is shown conclusively by the rank-order correlations.

To obtain adequate sample sizes, groups E and IE were combined and the boys and girls ranked separately according to the amount of creative play they had shown (by C. H.), and according to their originality scores (by R. B.). The Spearman rank-order correlation was 0.516 ($P < 0.05$) for boys and 0.368 (not significant) for girls.

On the personality questionnaire, the non-exploring girls rated themselves as apprehensive, tense, reserved and conforming; the boys in this category saw themselves as unadventurous and inactive. The creative girls rated themselves as assertive and independent, mostly outgoing and more often placid than

Table 1

	Numbers		
	NE	E	IE
Original study			
Boys	5	20	25
Girls	15	27	6
Present study			
Boys	3	10	10
Girls	6	14	5
Mean originality scores and standard deviations			
Boys	24.5 (11.3)	44.9 (21.7)	76.3 (29.6)
Girls	36.2 (15.8)	39.8 (16.3)	61.5 (20.2)
Significance of differences			
Boys versus girls	$t = 2.42$ $P < 0.05$	$t = 1.02$ n.s.	$t = 3.87$ $P < 0.01$
Boys	NE vs E $t = 2.78$ $P < 0.02$	E vs IE $t = 4.51$ $P < 0.001$	
Girls	NE vs E $t = 0.53$ n.s.	E vs IE $t = 2.45$ $P < 0.05$	

apprehensive. The boys, on the other hand, did not conform to a recognizable pattern: some saw themselves as tough-minded; others as tender-minded, some as phlegmatic, others as excitable; but most rated themselves as fairly independent and venturesome.

The parents' ratings were rather more difficult to evaluate, mainly because they tended to cluster around the middle or "neutral" point of the 5-point scale; when the extremes of the scale were used they were invariably the socially "acceptable" values. In this way, discrepancies arose between the ratings of the parents and those of the teachers, but only in two or three instances were they on opposite sides of the scale.

All three boys who were non-explorers were described as "not curious" by both teachers and parents. The girls in this category were said to be sensitive and easily discouraged, preferring sedentary to physical activities; they had difficulty mixing with their peers, and the concentration of three of them was said to be very poor. The IE girls were described as curious and independent; they mixed easily and concentrated well, but teachers found the classroom behaviour of two of them "undesirable". The boys in this category were most often described as very curious—they also mixed well and preferred physical to sedentary activities. The teachers, however, found them to be disruptive influences in the classroom, and parents tended to rate them on the negative end of the "calm and stable" scale.

In summary, the failure to explore in early childhood seemed to be related to lack of curiosity and adventure in boys and to difficulties in personality and social adjustment in girls. This interpretation is strengthened by the scores on the creativity tests: the NE boys scored considerably lower than the E boys, but there was no difference between the performances of the NE and E girls. Perhaps more important, a child's inventiveness and creativity in play were associated with his subsequent facility in divergent thinking. This association was greater and more direct in boys than in girls: that is, the more inventive the boy was in early childhood, the more divergent he was likely to be later on. This difference is not surprising since, even by the age of 4 years, girls are linguistically and socially more competent than boys¹⁴⁻¹⁷; their creativity therefore may be symbolic and covert, even involving sophisticated role-play which might not be very obvious to an observer. Boys, on the other hand, are actively exploratory for a much longer period of their life, and their activity is more explicit. In other words, though a divergent cognitive style is likely to be expressed in the play of boys, it may not necessarily be so in that of girls.

Nevertheless, the inventive boys turned out to be highly divergent thinkers, more so than the girls; they were also

socially less well adjusted than the inventive girls. Whether this is the stuff of which the creative artist or scientist is made remains to be seen.

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Effects of Marijuana on Recall of Narrative Material and Stroop Colour-Word Performance

Two recent articles^{1,2} report that marijuana interferes with the recall of narrative material learned in either a drug or no drug state and recalled in the drug state, but the evaluation of the results is hampered by (1) the lack of specification of the Δ^9 -THC content of the marijuana cigarettes and (2) an absence of placebo controls. We have set out to test the effects of marijuana on narrative recall and Stroop colour-word performance and to remedy these defects of experimental design. The Stroop test was selected because performance has been shown to be impaired by depressants such as amobarbital³ and because marijuana has barbiturate-like effects⁴.

Twelve paid volunteer students over 21 yr old served as subjects. All of them smoked cigarettes and several had some previous experience with marijuana, but neither chronic marijuana users nor users of potent hallucinogens were included. Subjects were randomly divided into two equal groups and were allowed to smoke either a marijuana cigarette (500 mg) calibrated to deliver a dose of Δ^9 -THC equivalent to 25 μ g/kg or a marijuana placebo cigarette, consisting of cannabinoid exhausted marijuana⁸. An observer was present to ensure that the cigarettes were smoked properly. Each subject smoked to a pre-set butt length within a 10 min period. All testing was performed in a double-blind fashion.

Thirty minutes after smoking began, an examiner read the Babcock Story and the subject was then asked to tell the examiner all he could remember about the story. Four degrees of increasing distortion⁵ were noted together with two other recall errors. The four types of distortion were (1) type *A* (weight of 1) which involved substitution of words with similar meanings or the use of vague terms; (2) type *B* (weight of 2) which consisted of a more radical type *A* distortion including the introduction of new elements; (3) type *C* (weight of 3) which involved the introduction of new material having an emotional tone which had no specific source in the original story; (4) type *D* (weight of 4) which involved the inclusion of arbitrarily unrelated material having a strong emotional tone which radically altered the story; (5) out-of-place memories which were recorded when some segment of the story was recalled out of its correct sequence and separated from its original place by a complete thought; (6) fragmentary memories were scored when a phrase or part of a phrase was remembered, but its relation to the story was lost.

After recall, Stroop colour-word performance was evaluated. Subjects were asked to view a screen on which a sequence of 100 words, 10 horizontal rows of 10 words each, were printed on a black background. Each of these words was printed in a colour which was unlike the word itself. Subjects were first required to read the words, and then to say the colour each word was printed in. Both the number of errors and the time to completion on each part of the test were the dependent variables.

Table 1 Effects of Marijuana on Recall of Narrative Material

Treatment	Distortions				Out of place	Frag-mentary	Memory units
	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>			
Marijuana	3.17	2.33	3.00	8.00	3.00	2.00	7.50
Placebo	3.16	2.00	0.50	1.33	0.66	4.67	12.00
	NS	NS	$P < 0.025$	$P < 0.025$	$P < 0.05$	NS	$P < 0.025$

The results of the Babcock-recall test are presented in Table 1. Differences between the marijuana and placebo groups on each of the distortions and memory units were evaluated by *t* tests. Marijuana treated subjects made significantly more type *C* and *D* distortions and out-of-place distortions. There were no significant differences on type *A* and *B* distortions and fragmentary memories. The controls also recalled significantly more specific memory units as reflected in the unit score differences.

Stroop test performance did not vary as a function of marijuana treatment. Although the time to read the words was significantly shorter than the time to read colours, there were no significant differences between the marijuana and placebo groups. Error scores also were not different.

Performance on Babcock Story recall in the present study generally supports Abel's findings. The memory deficits seen here, however, not only involved an inability to remember specific material, but also involved the introduction of material not originally included in the narrative. The intrusion of irrelevant associations in the recall of narrative material has previously been noted by Clark⁶. Whether memory distortion is due to faulty acquisition or an impaired ability to retrieve information cannot be answered from this study. Performance on the Stroop colour-word test was unaffected by marijuana. It is possible that higher doses of THC in the cigarettes might produce both depressant and psychotomimetic effects which would affect Stroop test performance. According to Callaway, depressants and psychotomimetic drugs broaden the attention span resulting in an increase in responsiveness to environmental stimulation⁷. The subjects' ability to filter out irrelevant stimuli would be thus impaired. Whether or not marijuana

can produce this effect can only be answered by increasing the dosage of Δ^9 -THC delivered in the cigarette smoke.

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Retardation of Discrimination Learning in Monkeys and Chicks Previously Exposed to Both Stimuli

WHEN animals are exposed to a pattern of stimulation they often learn its characteristics even though they are not rewarded for doing so¹. This has been demonstrated in rats and chicks by subsequently using familiar patterns as cues in a food-rewarded discrimination²⁻⁸. Usually perceptual experience makes subsequent discriminations easier for the animal. We now report that discriminations between two objects can become more difficult for an animal after it has been exposed to both of them.

Twelve immature rhesus monkeys (*Macaca mulatta*) were deprived of food and separately trained to press an illuminated panel in order to obtain a peanut; the automated discrimination apparatus had sixteen panels and patterns could be projected from behind onto any combination of the panels⁹. Next the monkeys were trained to discriminate between a square outline and a cross. The monkeys were matched in pairs on the basis of the number of trials taken to learn the task. Half of the matched pairs were simply exposed to the figures 2 and 5 placed 10 cm apart in their home cages and half were exposed to the figures 6 and 8. The figures were illuminated from behind and were identical in shape and size with figures which could be projected on to the panels of the discrimination apparatus.

After 50 days all the monkeys were separately trained to discriminate between 2 and 5 by rewarding a press at the figure 2 with a peanut in the automated discrimination apparatus. The expectation was that the monkeys with previous experience of the patterns would learn more quickly than those for whom the patterns were novel. But the opposite result was obtained; the monkeys which were familiar with both patterns took a mean of 336.0 trials to reach a criterion of 18/20 correct whereas the monkeys which had seen neither of them before took 130.2 trials. This result was so surprising that the experiment was repeated with some minor changes in design.

A fresh batch of twelve monkeys were pretrained and matched as before and then exposed to the letter M or the

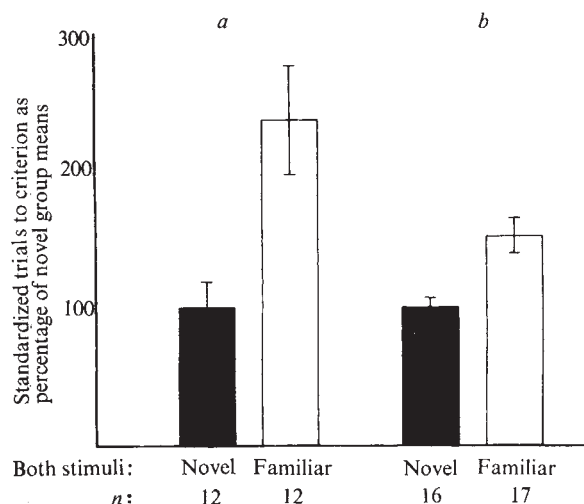


Fig. 1 Means and standard errors of the number of trials taken to discriminate between two stimuli by rhesus monkeys (a) and domestic chicks (b) previously exposed to both stimuli (open bars) and monkeys and chicks for which both stimuli were novel (solid bars). The results have been standardized as percentages of the means for the groups trained with two novel stimuli.

letters H and K in their home cages for 31 days. All letters were removed from cages before training began. Each monkey was required to discriminate between K and H by rewarding each press at K with a peanut. The monkeys familiar with both patterns took a mean of 320.8 trials to reach criterion whereas the group previously exposed to M took 149.8 trials. The results from the two experiments have been combined in Fig. 1 after each individual's score had been standardized as a percentage of the mean number of trials to criterion taken by the group unfamiliar with both stimuli in that experiment. The difference between the groups is highly significant according to the Mann-Whitney test ($P < 0.005$).

The second series of experiments were done with young domestic chicks (*Gallus gallus*) exposed to stimuli in an imprinting situation. The chicks were socially isolated throughout and were exposed for 1 h to moving cylinders each day for the first 5 days after hatching. Half the chicks were exposed to cylinders of one colour and half to two kinds of differently coloured cylinders. On the sixth and seventh days after hatching the chicks were food-deprived and pretrained to run down a Y-maze for a food reward. On days eight to twelve they were taught to discriminate between two stimuli placed at the end of Y-maze arms by rewarding an approach to one of the stimuli with chick crumbs.

In the first two experiments one group of chicks was exposed to both red and blue cylinders, and the other group was exposed to green. In the first experiment they were subsequently trained to discriminate between red and blue by rewarding an approach to red with food and in the second experiment an approach to blue was rewarded. In the third experiment one group was exposed to both blue and green stimuli and the other group was exposed to red. These two groups were then trained to discriminate blue and green by rewarding blue.

In the first experiment the chicks familiar with both stimuli took a mean of 32.8 trials to reach a criterion of 18/20 correct, while the chicks for which the stimuli were novel took a mean of 32.4 trials. In the second experiment, however, the chicks familiar with both stimuli took 45.5 trials and those familiar with neither took 20.8 trials to reach criterion; and in the third experiment the chicks familiar with both stimuli took 45.7 trials and the group unfamiliar with both took 31.4. The results of all these experiments have been standardized as described above and combined in Fig. 1. The groups familiar with both stimuli took significantly longer to learn the task

than the groups unfamiliar with both (Mann-Whitney test: $P = 0.008$).

The animals could be adversely affected by their previous perceptual experience regardless of whether one or both of the stimuli are familiar. The results of other workers⁶⁻⁸ and other experiments in the same apparatus (Chantrey, in preparation), however, indicate that a discrimination between a familiar and a novel stimulus is much easier for a chick to learn than a discrimination between two novel stimuli. So the retardation of learning described here depended on both stimuli being familiar.

We do not think our results should be interpreted in terms of the experimental groups having habituated to the familiar stimuli since the animals responded as quickly as those in the control group during training. Furthermore, both monkeys and chicks learn visual discriminations more rapidly than control groups when one of the stimuli is familiar to them. We suggest that in the experiments reported here the characteristics of the stimuli to which the animals were exposed were learned but were classified together since they occurred in the same context. Such a process would be expected to interfere with subsequent discrimination learning in which the animal had to classify the two stimuli apart.

While the phenomenon of classification-together is a hitherto neglected consequence of perceptual experience, it may be of considerable biological importance. The role of such a process is especially obvious in the case of imprinting. The young bird needs to learn the characteristics of a mother whose appearance can alter markedly as she changes her position in relation to the young—one moment presenting her back, the next facing them. If the young bird is to respond quickly and selectively to its mother after the attachment process is over, it must recognize her whatever position she adopts. The rules for the transformation from back view to front view must be very elaborate and unlikely to be comparable with the well known examples of perceptual constancies. We suggest that the different views of her are learned and subsequently treated as equivalent. The advantages of doing this are not restricted to the imprinting situation. Classification-together of physically different stimuli may well be necessary for some of the more complex examples of "concept formation"¹⁰⁻¹², even though abstraction of common features of different stimuli and generalization from familiar to novel stimuli are also likely to be involved. The process may also play a larger part in human perception than personal experience suggests—introspection between a poor guide to the distinctions which we ignore in our own classifications.

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Observations on a Living Coelacanth

DURING the recent Franco-British-American expedition to the Comoro Islands at the north end of the Mozambique channel we had the opportunity to observe a living coelacanth. The fish, a small specimen 85 cm in length, was caught by a native fisherman at Iconi, Grande Comore, at 0200 on March 22, 1972. It was caught from a pirogue by hand line, using a piece of tuna as bait. The fish was transferred by the fishermen to a cylindrical cage approximately 1.5 m diameter by 2 m length which had been built at Iconi during a previous Canadian expedition.

We arrived at Iconi at approximately 0340, by which time the fish was in the cage, grounded in shallow water. The fish was observed by the light of electric torches during the remaining hours of darkness; since it survived until 0745 it was possible also to watch and film it by daylight. For this it was transferred to a white glass-reinforced plastic tank.

During the period of observation the fish swam gently around the cage and the tank, and slow swimming movements were well seen. No rapid swimming movements were seen, nor did the gentle movements cease until the fish was moribund.

Forward propulsion was achieved by the concerted action of the second dorsal and anal fins. These were moved from side to side across the body with a sculling action. The fin was twisted on its pedicle so that its anterior edge led the movement, the lobe being oblique to the direction of movement and with a forward convexity like the blade of a propellor. For the return stroke, the twist was reversed; thus the anterior edge always led, but the right and left sides of the fin were functionally front and rear faces of the "propellor" on alternate strokes (Fig. 1). The second dorsal and anal fins moved synchronously, and to the same side of the body at the same time. Each of them moved through an angle of approximately 90°. During these movements, the two fins raked back from the longitudinal axis of the fish by an angle which varied between approximately 75° and 45°. The tail undulated from side to side slightly during these movements, but the undulations appeared to be passively induced by the movements of the fins. No sinusoidal body swimming movements nor active swimming movements of the tail were seen; the abundant body musculature suggests, however, that powerful tail strokes are possible.

The pectoral fins also performed sculling movements, but they moved independently of one another. Their movements were in the vertical plane, but their angles of twist and rake were not constant; their anterior edges led the movements, which were comparable with those of the second dorsal and anal fins. They did not appear to be concerned with forward propulsion, but with stabilizing and balancing movements. The pelvic fins were not seen to make any active movements, but trailed at an angle of approximately 30° to the longitudinal axis. The first dorsal fin was held in a half-erect position, and did not move actively.

Respiratory movements were not prominent; the mouth was held partially open, and irregular active closing movements of the operculum at intervals of approximately 20–30 s were seen. The head and jaws were watched carefully, but only feeble movements of these parts were observed.

During the period of observation the fish at no time rested on the bottom, so its behaviour in contact with a solid substrate could not be noted. Despite its gentle swimming movements the fish dived or approached the surface easily, the snout breaking the surface at times. Sometimes it became turned on one side, and swam so for several seconds; righting movements were made eventually, but were by no means immediate. A strong impression was gained that the fish was in a state of neutral buoyancy during life, though it just floated when moribund.

The eyes were seen to make only small movements, but their great passive mobility within the orbits, observed just after death, suggests that they are capable of more extensive excursions than were seen.

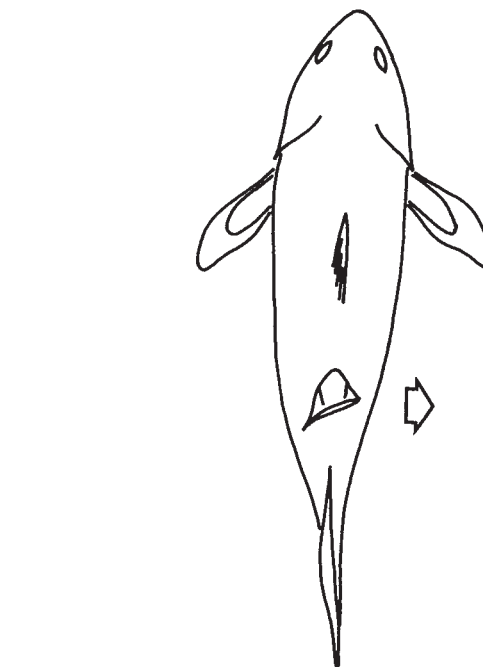


Fig. 1 Diagram of coelacanth as seen from above. The second dorsal fin is moving across the back in the direction of the arrow. It is drawn as if cut across, to show the curvature assumed by the lobe. The left side of the fin is the front face on this stroke; on the return stroke, the right side of the fin would become the front face. The anal fin would be moving in the direction of the arrow, synchronously and with the same action as the second dorsal fin.

The eyes exhibit a striking pale yellow eyeshine when illuminated, although no luminescence was noticed; the lenses were slightly cloudy, a frequent occurrence in fishes brought up from some depth, but both they and the corneae were seen to be colourless when the fish was subsequently dissected.

The colour in life was a uniform dark grey-brown, shot with an unsaturated bluish element, reminiscent of the colour of thin polythene sheet. Some pale patches, often seen in preserved specimens, were present; some of these seemed to have been caused by the displacement of some scales, although others were patches of pallor on an intact field of scales.

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Changes in Distribution of *Acanthaster planci* Populations on the Great Barrier Reef

POPULATIONS of the coral predator, *Acanthaster planci*, are changing their distribution on the Great Barrier Reef. Investigations before late 1969 indicated that it was commonest on reefs between 14° 40' S and 18° S¹⁻⁵ (see also Table 1). I have been studying *Acanthaster* since 1969, and have found that it has become less common in the north and more common further south.

For convenience, the Great Barrier Reef has been divided into six zones to show the known recent distribution of

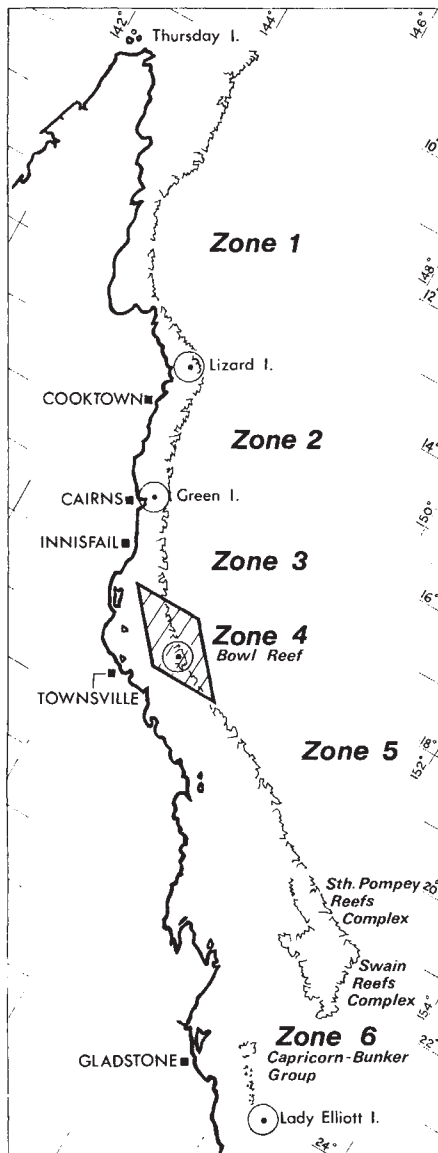


Fig. 1 Zonation of Great Barrier Reef with respect to *Acanthaster* distribution. Greatest populations of *Acanthaster* are currently in zone 4 (shaded).

Acanthaster (Fig. 1). Although few reefs have been examined in zone 1 (Thursdays Island, $10^{\circ} 35' S$, to Lizard Island, $14^{\circ} 40' S$), *Acanthaster* appears to be rare there, which is supported by other workers^{3,4}. In zone 2 (Lizard Island to Green Island, $16^{\circ} 46' S$) there has been a considerable decrease over the past few years in the number of reefs known to support infestations, that is, forty or more starfish observed per 20 min of searching. Coral mortality, considered attributable to *Acanthaster*, was patchy on individual reefs and varied in extent from reef to reef in the zone. Damage to corals was negligible on almost all of the outer barrier reefs. Few *Acanthaster* have been observed on reefs in zone 3 (Green Island to $18^{\circ} S$) since late 1969. This is in marked contrast to the results obtained previously⁵. Coral mortality is now extensive on many reefs.

Acanthaster populations were found to be greatest in zone 4 ($18^{\circ} S$ to $19^{\circ} S$), where reefs were surveyed in November–December 1970, just before the breeding season⁵, and again in May–June 1971. While data on recruitment were inconclusive, indirect evidence was obtained at Bowl Reef to add further support to the view that adult starfish move between reefs^{2,5}. No starfish were observed on this reef in November 1970, whereas 314 were observed during June 1971, of which only two specimens were estimated to be less than 30 cm in

diameter and most were estimated to be 40–50 cm. Almost all starfish were found together on a small section of the back reef slope in 12–16 m. They were feeding on corals and there were many recently killed corals in deeper water nearby. Elsewhere on the reef there was no evidence of unusual coral mortality. These observations suggest that starfish have only recently appeared on Bowl Reef and that they are moving up the reef slope from deep water. The general impression gained was that coral mortality on reefs supporting infestations in zone 4 was comparable with that observed on reefs further north which supported infestations about five years ago.

Table 1 Changes in Distribution of *Acanthaster* Populations

Zone	Latitudinal range	Before August 1969*					
		No. of reefs†	Reefs visited	No. of censuses	Reefs infested‡	Reefs partially infested§	% Infested or partially infested
1	$10^{\circ} 35' - 14^{\circ} 40'$	437	6	10	0	0	0
2	$14^{\circ} 40' - 16^{\circ} 46'$	139	37	94	10	10	54
3	$16^{\circ} 46' - 18^{\circ} 00'$	51	22	67	11	5	73
4	$18^{\circ} 00' - 19^{\circ} 00'$	63	10	34	3	1	40
5	$19^{\circ} 00' - 23^{\circ} 00'$	666	14	26	0	0	0
6	$23^{\circ} 00' - 24^{\circ} 07'$	22	3	11	0	0	0
Total		1,378	92	242	24	16	44
Zone	Latitudinal range	Since August 1969					
		No. of reefs†	Reefs visited	No. of censuses	Reefs infested‡	Reefs partially infested§	% Infested or partially infested
1	$10^{\circ} 35' - 14^{\circ} 40'$	437	0	—	—	—	—
2	$14^{\circ} 40' - 16^{\circ} 46'$	139	38	157	0	2	5
3	$16^{\circ} 46' - 18^{\circ} 00'$	51	24	72	1	4	21
4	$18^{\circ} 00' - 19^{\circ} 00'$	63	37	254	23	3	70
5	$19^{\circ} 00' - 23^{\circ} 00'$	666	3	17	0	0	0
6	$23^{\circ} 00' - 24^{\circ} 07'$	22	13	63	0	0	0
Total		1,378	115	563	24	9	29

* From Table 2, ref. 5.

† Approximate totals only, as some areas poorly charted.

‡ 40.0 or more starfish observed per 20 min of searching.

§ 10.0 to 39.9 starfish observed per 20 min of searching.

Only three reefs in zone 5 ($19^{\circ} S$ to $23^{\circ} S$) have been examined recently and they were in the region $19^{\circ} S$ to $19^{\circ} 30' S$, where *Acanthaster* was rare. The few data available from other areas in this zone indicate that in the South Pompey Reefs Complex and the Swain Reefs Complex *Acanthaster* is rare^{3,5}. In zone 6 (Capricorn–Bunker Group) small populations of adults, but no juveniles, were observed in the lagoons of reefs in the Bunker Group. Each population appeared “in balance” with the surrounding reef corals. Further study of these populations seems warranted.

In view of the evidence that adult starfish probably move between reefs, together with the changes in distribution shown in Table 1, it seems that *Acanthaster* is moving southward.

I thank Professors J. H. Connell and J. M. Thomson for advice, J. Bloomfield, Julie Henderson, and D. Ada for their assistance on the surveys and the Queensland Government who financed the study.

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³ Weber, J. N., and Woodhead, P. M. J., *Mar. Biol.*, **6**, 12 (1970).

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BOOK REVIEWS

City Studies

Metropolitan Problems. Edited by S. R. Miles. Pp. xx+534. (Methuen: Toronto, London, Sydney and Wellington, April 1971.) £7.

THIS is a survey of metropolitan problems the world over, based on an international seminar held in Toronto in 1967, under the auspices of the Ontario Bureau of Municipal Research. It has been skilfully edited by Mr Simon Miles, the Executive Director of the International Association for Metropolitan Research and Development, who has linked together fifteen separate essays by a series of bridging notes, and has himself contributed key chapters on the constituents of and solutions to the problem of the metropolis itself. Assessments are made of population, housing, health and welfare, transportation, and administration, and then the book passes to the problems of development including financing, planning, government and management.

The principal contribution of the book is its comparative approach, comparing metropolitan growth in developed and developing countries, and in major geographical regions such as Anglo-America and Western Europe, Australia, the USSR and Eastern Europe, Asia and Africa, and Latin America. Its themes are not new: in becoming a city dweller man is imposing strains on his nature, as well as on Nature itself; physical expansion has outrun social and especially administrative growth; increase in technology increases discord; and, to parody Lin Piao, man's capture of the city has strangled the countryside. The theoretical content is disappointing and consists in frustrated attempts at broad categorizations based on putting together unique instances. The descriptions of how common problems are variously met are, however, interesting and valuable. As a compendium of information on a hundred or so metropolitan communities it should stimulate thought on how better to do things *here* because they are handled so much more effectively *there*! However, no very

clear ideas of sociological structure or geographical pattern come out; if anything one tends to be bewildered, if not lost, in the array of individual cases.

Part of the metropolitan problem is its magnitude. A hundred years ago, in 1870, only 1 per cent of the world's population lived in cities of more than a million; today more than 12 per cent do, and by the year 2000, 21 per cent may—thus crowding more than ever the already overcrowded parts of the world. Size has become unmanageable. Central cities within metropolitan areas have grown obsolete, while peripheral ones have little to say for them except their newness. Cities have outrun their frames of reference, and though they have come to dominate their regions they have not had those regions under their control. Much attention is devoted to the need for much more widely based regions for planning, government, and development—although the logic of this has not been pressed to its conclusion, which might lead, for example, to the decision to scrap Maud and Wheatly as already outdated and divide Britain into the five administrative regions of London, Birmingham, Manchester, Leeds and Glasgow.

The pace of expansion is also constantly stressed as a major problem. The metropolis has a space-age technology but a stone-age mind. The car is banned or slowed down or made less of a convenience because of unimaginative road engineering and ineffective road management. Changes in social mores are impeded by institutional inertia, particularly by outmoded political institutions. Class and ethnic divisions are entrenched because the school system is hidebound. In many cases planners plan as though they regretted the urban age, and wished to bring back the village into the exploding metropolis, seeming to deny the basic attraction of the city, an attraction that has caused the greatest single revolution in the past century and a half. One writer even has to remind us, "One cannot halt urbanization"—as though to do so had been the ideal to be aimed at.

Another problem constantly harped

on has been the fragmentation of the metropolis, broken as most large cities are by geographical handicaps not adequately overcome, by social divisions, especially race and status, not sufficiently bridged, and by political piecemealness, not curbed at all effectively. Almost every writer has urged the need for more control, more integration, and more unity, with more powers over transport, utilities, education, and administration in metropolitan hands.

The unequal evolution of great cities as between the developed and developing cities comes constantly to the fore: western countries are concerned about urban renewal, building houses with a room per person, and planning roads for the two-car family, when Asian and African lands have to plan for the basic elements of existence and survival. For metropolises in the developing lands to come up to their western counterparts an enormous back-log of housing, schooling, hospital construction and roadbuilding has to be made up, yet they have not the means to do this. Housing investment in India is only 2 per cent of the GNP compared with 5 per cent in Western Europe. Disparities in schooling are even greater. By AD 2000 Bombay may well reach a population of 9.5 millions, by which time it will be in need of 3,240,000 school places, requiring 55 square kilometres of land, an almost impossible objective. Yet Asia is being swept by "a revolution of rising expectations" which will not brook the indefinite postponement of parity in development. Obviously senior governments at the national level and international agencies will have to do more to assist in metropolitan growth—and in the management of that growth.

In all this, as Mr Miles concludes, there will be a much greater need for planning—for the clarification of planning principles and the improvement of planning techniques—and also for the formulation and communication of planning goals. His summary chapter is a brilliant estimate of the handicaps still to be overcome yet the opportunities still offered us in measuring up to

the metropolis—the acute expression of man's greatest problem today, the increase of mankind. This is a study which all social scientists, indeed all those concerned about the future of population and settlement, certainly should secure.

J. W. WATSON

"New Naturalist" Ecology

Woodland Birds. By Eric Simms. Pp. xxii+391+28 plates. (Collins: London, November 1971.) £3.

Mountains and Moorlands. By W. H. Pearsall. Pp. 321+81 photographs and 46 maps and diagrams. (The New Naturalist.) Revised edition. (William Collins: London, January 1972.) £3.15.

In the debate as to whether we are or are not on the edge of an ecological catastrophe, it is equally unprofitable to dismiss the predictions of thoughtful scientists as seeing "catastrophe in the tea leaves" (*Nature*, **235**, 63; 1972) as it is to espouse the fashionable and often ill-thought-out view that disaster is imminent with insufficient understanding of ecological concepts. What is needed by almost everyone is a great deal more knowledge of the detailed workings of the natural world and in particular of the impact which man is having and has already had upon his environment.

These two publications in the Collins "New Naturalist" series both help to provide this understanding. Both dispel woolly ideas about all living things being vaguely interrelated and provide instead a detailed factual account of the geological, climatic and biotic factors that determine the distribution and abundance of living things in two different habitats.

Reading Eric Simms's book *Woodland Birds* is like being taken into a wood by a really knowledgeable expert with a lifelong experience and love of birds. A large amount of factual information, much of it based on the author's own observations, is interspersed with occasional and entirely apt touches of poetry. Mr Simms describes the origins of woodlands, birds in different sorts of wood and in developing woodland and the factors that regulate bird populations. There is a particularly interesting chapter on bird song in which he gives detailed measurements of the fine structure and length of various songs. The song of the great spotted woodpecker, for example, consists of drumming with the bill against a tree, and half a second's worth of drumming consists of as many as eleven beats. Imitation of the notes of other species is a surprising phenomenon. The author himself was completely deceived by a great tit's rendering of a nuthatch call. In a chapter on birds in towns,

Mr Simms points out that many of the birds which have been most successful in adapting to towns and cities are basically woodland species, the black-bird, which has spread remarkably in recent years, being a prime example.

A feature of woodlands which emerges from this book is their vulnerability to the actions of man, even when human populations are relatively small. About 90% of our native forests have been cleared since Neolithic times and the number of trees and hence of woodland birds is heavily dependent on the whims of man in planting or felling.

Mountains and Moorlands by the late W. H. Pearsall is a new edition of a "New Naturalist" publication which first appeared in 1950. It has been revised, but only to a small extent, by Winifred Pennington (Mrs T. G. Tutin). She has revised the chapter on the history of the upland areas as considerable new evidence has come to light through radio-carbon dating techniques. She has also added a chapter on the activities of the Nature Conservancy, a body with which Professor Pearsall was much concerned.

We tend to think of mountains as a most stable feature of our landscape and it is therefore at first sight surprising to find that one of the dominant themes of this book is change. The surface of upland areas is continually being broken up by freezing and thawing, eroded by wind and water. Trickle of stones and rock falls testify to this continual change. Less obvious is the fact that the vegetation too is changing. Professor Pearsall provides evidence that much of what is now moorland was once covered with trees and points out that grazing animals cropped as flesh or wool are a constant drain on moorlands, gradually changing them into less fertile areas.

Professor Pearsall argues that these facts of change should have considerable bearing on the formulation of policies of conservation and land use, since if the uplands are degenerating communities then it is questionable whether we should struggle to retain them as they are. The emphasis of the book is botanical, reflecting Professor Pearsall's own interests, but there are also chapters devoted to geology, climate and the animals of the moorland. The book is indeed a remarkable synthesis of different areas of knowledge.

MARIAN DAWKINS

Quantum Electronics

Progress in Quantum Electronics. By J. H. Sanders and K. W. H. Stevens. Vol. 1. Pp. vii+374. (Pergamon: Oxford and New York, December 1971.) £7.

THIS is the first of a series of volumes containing review papers in a field very

loosely described by the words "quantum electronics". The editors admit in the preface that no one has a satisfactory definition for the field covered by the term, and some papers, at least, will, therefore, not be of much interest to any one reader. Of the five chapters or review papers in this volume, four concern lasers or topics closely allied with the application of lasers. The fifth has no connexion with lasers whatever, which is not to say that the paper is not interesting in its own right.

The first paper, by A. Yariv and J. E. Pearson, is on parametric processes. In this relatively short chapter, the authors develop a concise treatment of the theory starting from first principles. The presentation is very clear and in a form that should make the paper useful to the novice as well as to the experienced researcher in the field. I heartily recommend it as tutorial reading for anyone working with parametric devices, whether in the optical or microwave region.

The next chapter is on light propagation and light shifts in optical pumping experiments, by W. Happer. The optical pumping experiments referred to here are the combined optical-radio-frequency resonance or magnetic moment orientation sorts of things that were originated by A. Kastler and his school in the 1950s, not the optical pumping that is used in lasers—this is the paper that has no connexion with lasers. In the first few pages, the author develops a very general and abstract theory of the interaction of resonantly absorbed light with the optically pumped vapour. This culminates in an equation the terms of which, individually, predict the various effects that may be expected in these experiments—resonant absorption, anomalous dispersion, Faraday rotation, birefringence and others, sometimes modulated at high frequencies. The reader who has only a passing interest in the subject is advised to skip the theoretical pages and go on to the descriptions of the effects, where he may marvel at the inductive ability of the author to predict them from the equations. Some of these effects have not yet been observed experimentally. The reader whose interest is in the device applications of optical pumping (for example, rubidium frequency standards) will find that this paper does not greatly enhance his understanding of these devices.

There follows a chapter on non-resonant feedback in lasers, by R. V. Ambartsumyan, N. G. Basov, P. G. Kryukov and V. S. Letkhov. Non-resonant feedback occurs when there is no distinct mode structure, but the authors approach the problem from the viewpoint of a resonator having many modes—so many that their resonances

overlap and interact strongly with one another. Since the threshold for this type of laser is quite high and the output not always very coherent, non-resonant-feedback lasers are not seen often in the laboratory; however, the theory has astrophysical applications.

A chapter on the semiclassical theory of the gas laser, by S. Stenholm, combines in one unified presentation much of the theory published originally in a famous paper by W. E. Lamb, jun., and extended by others. This chapter, like the first, can be recommended highly for its tutorial value. It starts from first principles and can be used by the novice with a knowledge of quantum mechanics, who will find it rough going at first but well worth the effort. A key point in the paper is the comparison of results obtained by two computational methods—the rate-equation approximation and perturbation theory. Unfortunately, the direct comparison is made with two equations that do not appear to be comparable: one clearly predicts the well-known power dip or Lamb dip, while the other, as far as I can tell, does not. Apart from this slip, the presentation is very complete and logical, and easy to follow.

The last chapter is a tabulation of known atomic gas-laser transitions, by C. S. Willett. It is organized according to atomic species and is not intended as a dictionary of gas-laser transitions—such tabulations have lost much of their former usefulness with the availability of continuously tunable lasers. Rather, the material is presented so as to emphasize the physics of the processes that give rise to laser action. There are brief remarks at each transition regarding the discharge conditions under which laser action has been observed, and profuse references to the source literature. The article makes an excellent companion to the theoretical paper that precedes it.

The over-all quality of the papers in this volume is uniformly high. It is to be hoped that the editors can maintain this standard in future volumes.

ARNOLD L. BLOOM

Muscle Science

Machina Carnis: The Biochemistry of Muscular Contraction in its Historical Development. By Dorothy M. Needham. Pp. xvi+782. (Cambridge University: London, December 1971.) £18; \$55.

SCIENTISTS have short memories. Too often clear trails are neglected for many years while the scientific pack bays after some false scent. For example, as Dr Needham says of Veratti's descriptions in 1902 of the sarcoplasmic reticulum, "It has amazed the later workers in this

field that work so accurate, elegant and interesting could have been forgotten within ten years and not rediscovered for another forty years". A few pages further on we read Claude Bernard's beautifully clear description of rigor without the formation of lactic acid, and learn how this knowledge was lost for fifty years, while the lactic acid theory of muscle action held the stage. There are many other examples. We should therefore be grateful for Dr Needham's valuable book which should help to reduce the forgetting certainly going on today, a situation compounded by the fact that so much is not forgotten, but simply never noticed in the tide of publications sweeping our desks.

Dr Needham presents us with an unusual work, a history of muscle science. The "biochemistry" of the sub-title is interpreted widely, and one is aware of the concern, running through the whole book, for biological understanding of how actual muscles work. The details of biophysical or biochemical experiments are never allowed to obscure this theme. The book includes, besides the obviously "biochemical" subjects of muscle proteins and muscle metabolism in contraction and in recovery, discussion of excitation, excitation contraction coupling, the ultrastructure of muscles, theories of contraction, comparative studies of vertebrate and invertebrate muscles, some aspects of muscle disease and a final chapter on contractile proteins in non-muscular functions. Within each section the treatment is historical. As I understand it, the objective is to show the development of knowledge, presenting the work of each investigator in its historical context, although illuminated by modern views of the subject where necessary. The figures are all reproduced from papers and aim to present results rather than to compare (or contrast) them. The book is thus neither a textbook nor a review, aiming neither to teach nor to put forward a personal view or new synthesis.

The text can be quite hard to follow unless one has a reasonable grasp of the subject to start with, and often one longs for a more critical synopsis and for more of Dr Needham's opinions as to the merit or significance of particular observations, methods or interpretations. Definitions of terms used are in short supply too. For example, I could find no definition of "efficient"; the term seems to be used in the unhappy sense that any process may be said to be "inefficient" in proportion to the heat it produces. Elsewhere, however, it is clearly explained that enthalpy and free energy changes are not necessarily equal (although the significance of this is hardly discussed). Where

appraisals do occur they often seem to me too uncritical, particularly where modern work is concerned. Although Dr Needham condemns the reluctance of the Meyerhof group to accept, and correctly interpret, the fact that much of the lactic acid formation in active muscle is postcontractile, she has no comment on the possible significance of the postcontractile phosphocreatine splitting several workers have reported. Nevertheless the awkward facts are there in her text—it is up to us to "treasure our exceptions" and try to interpret them.

A work such as this obviously needs an extensive bibliography. One's hopes are more than fulfilled by the 3,000 or so references, all given in full. About three-quarters of these are to work in the last 25 years, comparatively few to work since 1968. Not many reviews are included. There is also an index of authors cross-referenced to the bibliography, a most useful feature. The subject index is less satisfactory—for example it contains no entry for phosphocreatine, a substance much discussed in the book. Of course even such a substantial work cannot be complete and it is always possible to criticize it for omissions. I personally cannot restrain a protest at the absence of any reference to work on muscle (especially its heat production) by Aubert and his collaborators in Louvain over the last 20 years.

In her preface Dr Needham expresses the hope "that in spite of its defects and omissions this book will be useful to some of those for whom the fearful and wonderful phenomena of muscular movement retain all their fascination". Certainly I have learnt much from it that I ought to have known already and shall continue to find the book indispensable. I am sure it will not only be useful to any muscle researcher but also help many of us to capture or retain the fascination Dr Needham refers to.

ROGER C. WOLEDGE

Marine Life

Life in the Sea. By Gunnar Thorson. Translated from the Danish by M. C. Meilgaard and A. Laurie. Pp. 256. (Weidenfeld and Nicolson: London, January 1972.) £2.10 hardback; £1.05 paperback.

THIS book, Mrs Ellen Thorson writes, is "my late husband's final contribution to marine biology". It is impossible to review it without having its author constantly in mind with his intense love of marine invertebrates and his infectious enthusiasm for all that concerned the sea. Something of this is conveyed here to a much wider public than could be

reached by his scientific papers or even his numerous lectures in so many countries.

In the first chapters the sea is regarded as a habitat for plankton, nekton and benthos, ranging downward from the photic zone above through the twilight and deep sea zones. Later the reader is taken from the intertidal with its diverse wealth of life progressively lower over the floor of the continental shelf and slope eventually to the profound depths of the ultra-abyssal or hadal zone.

Gunnar Thorson is happiest in these depths among members of the level bottom communities to our knowledge of which he contributed so greatly. The reader constantly encounters illuminating comments from the wealth of unique experience. Only when dealing with coral reefs, where he had minimal experience, is this personal touch missing. But the sole error noted—*Lima excavata* does not swim or form abyssal nest—concerns an inhabitant of the Norwegian fjords.

Particularly notable are the illustrations, both drawings and photographs. Some of the more delightful of the former will be recognized by the numerous recipients of Gunnar Thorson's Christmas cards, made by Kai Olsen of the Helsingør Marine Laboratory, largely of invertebrates there observed.

The economy of marine life is presented in terms of its contributions to human nutrition. Professor Thorson is none too optimistic about future prospects but emphasizes the extent of our ignorance and the need for more marine biologists, many of whom may find first stimulation in the reading of this most admirable book.

C. M. YONGE

African Butterflies

Tropical Butterflies: The Ecology and Behaviour of Butterflies in the Tropics with Special Reference to African Species. By D. F. Owen. Pp. xiv + 214 + 40 plates. (Clarendon: Oxford; Oxford University: London, November 1971.) £4.25.

THE introductory chapter of *Tropical Butterflies* is written with a casual enthusiasm that stimulates further reading. The author has spent several years studying butterflies in East and West Africa and has drawn together his own studies and presented them in a more general biological context in an up-to-date summary which emphasizes ecology, genetics, evolution, and behaviour. Other subjects covered include classification and zoogeography, life histories, species diversity, seasonal abundance, mimicry, and migration, together with one chapter each on

methods of study, agricultural implications, and conservation. The book focuses on African species. The population ecology of *Acraea encedon* raises many important questions, and suggests that man's activities in reducing the complexity of the African environment through overpopulation and excessive agriculture may be unbalancing the sex ratio of the species, a subtle road to possible extinction.

Much of the impact of the author's points is based on colour differences which are obscured by black-and-white photographs; only one of the forty plates is in colour. Figs. 6 and 9 of plate 29 are switched, and the omission of identifying labels on Fig 9.1 makes correlation with Fig. 9.2 difficult; but the layout is excellent and the quality of the figures is high.

The main contribution of this book is in bringing together a great deal of African butterfly natural history and combining it with a summary of recent research on the more important aspects of tropical butterfly biology. The author does not develop new generalizations, nor does he delve critically into many of the subjects discussed, largely as a consequence of limiting the references almost solely to work done on a single group of organisms. Nevertheless *Tropical Butterflies* is an important contribution with appeal to amateurs and presents several aspects of interest to professional biologists.

LINCOLN PIERSON BROWER

Transuranium Elements

The Chemistry of the Transuranium Elements. By Cornelius Keller. Vol. 3. Pp. xv + 675. (Verlag Chemie, Bmbh: Weinheim/Bergstr, 1971.) 188 DM.

THESE 675 pages of carefully and concisely worded prose are a monument to the progress that has been made in understanding the properties of the transuranium elements during their short thirty-year history. They present a remarkably complete, up-to-date compendium of the chemical properties of these elements. More than that, they include much on their physics, history, methods of production, and practical uses.

The book is divided into two parts. The first part includes a comparative treatment of the chemical and metallic properties of all of the actinide elements—thus including thorium, protactinium and uranium. The properties of the actinide elements are correlated to some extent with their lanthanide (rare earth) homologues. Also treated briefly are the physics of nuclear synthesis, structure, and radioactive decay; the electronic structures; the methods of small- and

large-scale production and purification; and some of the practical applications.

In the second part, the chemical properties of each of the 13 transuranium elements (neptunium to hahnium) known at this time are discussed individually in a systematic way. Descriptions of the discovery, isotopes, methods of purification and metallic properties (where known) are included.

Predicted electronic structures and chemical properties of transactinide and the projected superheavy elements, and periodic tables—with a fascinating one extending up to atomic number 218—are included. Such useful information as the masses (and related information) of the isotopes of elements from lead to element 108, X-ray energies of all the actinides, and maximum permissible concentrations (from the health viewpoint) of radium and the actinides are listed in the appendix. A total of nearly 2,000 references covers the more recent literature on the chemistry of the transuranium elements quite well.

As is inevitable in a comprehensive work of this type, the experience and predilections of the author lead to greater emphasis and better treatment in certain areas. Thus the chemistry is on the whole much better than the physics, as might be expected from the title of the book. The crystal structure, coordination compounds and the metallic state of the actinide elements are treated exceptionally well. The oxidation-reduction reactions and equilibria between ions, and in general the chemistry of the ions in aqueous solution, are covered less completely. The treatment of the electronic and magnetic properties and the correlation of trends in the chemistry of the elements from the viewpoint of changes in the electronic structures are likewise less adequate.

There are a number of minor errors, more in the physics than in the chemistry, but not enough to detract from the overall excellence of the book.

This book should be of value to the non-specialist and student of chemistry. It should also be of value to the laboratory chemist. Methods and conditions for oxidizing lower oxidation states (with corresponding colour changes) and optical spectra useful for identification of various oxidation states are given, as well as detailed methods for the separation and purification of the elements. Even the relatively recent field of the organometallic chemistry of the actinides is covered.

This book fulfils a definite need. The last comprehensive book on the chemistry of the actinide elements was published 15 years ago. The translation from the German is excellent, as are the illustrations and the quality of the paper on which the book is printed.

GLENN T. SEABORG

CORRESPONDENCE

Population Stability

SIR,—A number of books, articles and letters have been published in recent months expressing concern at the threat of over-population. I refer, for example, to the letter signed by fifty-two doctors in the *British Medical Journal* of January 8, 1972, that made a series of recommendations "to combat the British disease of over-population" and to the recent work of Professor Meadows initiated by the Club of Rome¹. How far do recent trends in population confirm the importance of this threat?

Two recent numbers of *Population et Sociétés*² show the crude birth rate trends since 1960 for twenty countries of Europe and also the birth rates necessary for long term replacement of the population. The birth rate is shown as having fallen by 1970 below replacement level in Denmark, Finland, West Germany, Portugal and Sweden in Western Europe and in Czechoslovakia and Hungary in Eastern Europe. The birth rate is shown to be still above the replacement level but to have been falling since 1964 in Austria, France, East Germany, Holland, Italy, Switzerland, the United Kingdom and Yugoslavia.

In England and Wales the number of births during the first 12 weeks of 1972 was 176,588 compared with 193,770 during the same period of 1971, a fall of over 8.8% in 12 months³. The decline in the birth rate that began in 1964 is continuing.

The crude birth rate for these first 12 weeks of 1972 was 15.6 per 1,000 population. The birth rate is in an average year 0.6 higher in the first quarter than for the year as a whole so that the 1972 crude birth rate could be no more than 15.0. *Population et Sociétés* shows a crude birth rate for the United Kingdom of about 14.0 as necessary for population replacement. If the present trend continues the United Kingdom could join the other countries with a fertility below replacement level in 1973.

The Government Actuary's latest 1970 projection leading to a population for the United Kingdom of 66.040 millions in the year 2000 assumed a virtually constant fertility or average completed family size of 2.4 for the next 30 years⁴. The fertility has already fallen below this assumption and Euro-

pean experts are forecasting that fertility will decline further⁵. If this happens then Austria, East Germany, Switzerland, the United Kingdom and Yugoslavia will soon join the other countries with a birth rate below the long term replacement level.

All the countries of Western Europe have shared the experience of a declining birth rate since 1964. The decline has also been proceeding in Canada, the USA and the USSR since the 1950s. There appear to be few grounds for assuming that this decline has now spent itself in the United Kingdom, or in any other developed country, particularly as the decline has recently accelerated. Projections based on a more stable and higher birth rate than we are now experiencing are of doubtful value as forecasts.

There were good grounds in 1964 for fearing the future over-population of developed countries. However, it is difficult to see that there is any threat of over-population today anywhere in the developed world.

Yours faithfully,

A. H. A. WYNN

9 View Road,
Highgate, London N6

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SIR,—In the course of your leading article "Another Whiff of Doomsday" (*Nature*, 236, 47; 1972) you comment that the population of Britain has gone through stages which have produced a situation which, "taking one decade with another can only be called stability".

I am at a loss to understand what data led you to make this assertion. I append figures taken from two Government publications, the Department of the Environment's *Long Term Population Distribution in Great Britain—A Study*, 1971, and the Government

Actuary's *Population Projections 1970-2010*, 1971.

	Population of Great Britain (thousands)	% Change over previous decade
1901	37,000	+12.0
1911	40,831	+10.4
1921	42,769	+4.7
1931	44,795	+4.7
1941	No census in 1941	+9.1
1951	48,854	
1961	51,380	+4.9
1971	54,563	+5.8

and estimates for the decades to follow, based on the 1969 situation

1981	57,254	+4.9
1991	60,538	+5.7
2001	64,505	+6.5

This is certainly a picture of stable growth, but hardly one of stability. I would not have thought it was possible to ignore the significance of adding 3 million affluent people each decade to a country which is already among the most densely populated in the world. You may, of course, believe that the growth predicted for the next three decades will not happen. This would be more credible if there were any sign of a long-term trend towards smaller families. In fact completed family size in the affluent world now tends to fluctuate with economic circumstances. Myra Woolf in her recent survey *Family Intentions* (HMSO, 1971) found that, in the present circumstances, the average desired family size was 2.5 (very close to that actually observed). However, when asked to select an ideal family size given no economic constraints, the average person chose 3.4. If we obtain the earnestly-pursued economic growth on entry to Europe it is possible to argue that the birth rate will rise as it did during the "Supermac" era.

Affluent people use birth control extensively, but this is not population control, nor can it become so unless we use every means at our disposal to change people's view of the relationship between the human population and the world which supports it.

Yours faithfully,

AUBREY MANNING

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Edinburgh EH9 3JT

Much depends on what is meant by population stability. If the total size

of a population is to be indeed constant, the net reproduction rate must be less than 1.0. But stability may in many eyes be preferably defined as net reproduction rate=1.0.—Editor, *Nature*.

Concern and Hysteria

SIR,—Since your criticism of the assault by environmentalists (*Nature*, 235, 63; 1972), the controversy has spread. For spectators like myself, who may be likened to keen supporters in the stands, the game being played seems to be so loaded with effects that we cannot be certain which side to support or exactly what the rules of the game are. What is certain is that if the pessimists are going to win, or even if the result is a draw, the worldwide result means drawn curtains in many countries of the globe.

Instead of waiting until the turn of the century to decide about the result, an objective look at the world now, from my luxurious position in a safe seat, causes some doubts in my mind. As I read the Sunday papers I learn about the present situation in Bangladesh. We all know in our secure countries of Europe that nothing will be done to alter the misery of those thousands of poor people. And nearer home we can watch the Irish play their revolution game, knowing that neither side will be any better off when it's all over, like Bangladesh but not quite so horrendous. The Irish have cause to remember their history and the death of thousands during the potato famine, but it has no real bearing on present quarrels except to show that the futile death of thousands in misery is easily accepted by the rest of the world. Lessons are not learnt through sacrifices of the poor, who are easily placed in a position to suffer by the limited imagination and false ideals of their educated leaders.

Could my grandchildren become such victims of a conflict or decline in our society? If they are to be safe, what is the price we are paying, or are we stealing their safety? By stealing I mean the "poor nations' bad deal" and feel worried by the threats made recently at the Santiago conference by Dr Salvador Allende, speaking at the UNCTAD III for the whole of the third world.

Apart from our moral position in relationship to the rest of the world we are in some danger of running out of essential supplies of phosphate for food production in 30 years and water in a much shorter time, according to Professor Borgstrom, accentuated by a lack of agricultural scientists and support teams for food production, according to Professor Borlaug, who says that planning often fails to become action in the field.

Surely to minimize the danger of

future disintegration in society happening in a variety of ways throughout the world, is taking up a responsibility for consequences that should make even the most optimistic scientist hesitate, before committing his ideas to publication. Your editorial seems to have had more effective influence and been more widely read than the many separate statements made by various experts in the sciences concerned with these ecological developments. Even my local MP was able to quote it as a form of reassurance to me!—adding that it was up to people like me, the average citizen, to do something about the situation. Quite rightly he stated that politicians can only legislate when public opinion is in favour of such developments and action. So your reassurance of the future is as effective as the calm voice of the captain telling us that everything is under control as the ship is foundering in some strange invisible storm.

Every authority I've read to date concerned with environmental developments believes very positively that the solutions can be found through "education". As this is my special area for action I would like to know who the educators are, and when and where do they operate? The communication of ideas of an abstract nature limits the teaching situation at every stage, and the requirements of any academic or scientific syllabus also prevent abstraction in depth, as your scientific readers must realize. Yet the ecological future of our world and its future problems has this science-fiction content that makes it very difficult to approach, except in a most abstract or imaginative way. For, as you say, there is no positive means by which statistics, meaningful or otherwise, can be related to life, now and in the future. The ease with which pupils and students and teachers can accept, take for granted or become bored with information and ideas is one of the educational problems facing ecological educators. Even the ROSLA Panels considering environmental issues were loath to give any undue preference to ecology as a special subject. In my experience people in society do not want to consider abstract changes. Only when rupture of society is affecting their position do they feel enough motivation to act. Even warnings of positive changes about to happen in the near future do not seem to penetrate the "apathy" or tranquillity of the individual generally, as is happening in the new rise in local rents and rates. Only when the bill is paid are complaints made, and if voices are silent until we are making payments for the bills threatened by some ecological scientists it seems we will discover too late that we cannot afford the price. We may have spent too freely in the past, we may not have saved up enough to cover

the cost, or we may have other changes we did not expect. Whatever reason, the prospect of these debts worries me and I would like to believe that science, technology and government are combining to plan responsibly so that I and my family, and the families of the world, have some future security.

Can this be achieved by educational methods? My own experience gives me feelings of doubt because it seems all the action comes from intellectual minority groups and the dull resignation of the average person or student seems an impenetrable barrier. And if legislation only happens when the majority are in favour of changes, then popular opinion will prevent politicians from making unpopular acts. This seems the great weakness of the first issue of the "Blueprint". Even the British Humanists Association's "People First", containing as it does such weighty evidence against any kind of complacency towards worldwide conditions of deterioration of civilized standards and disintegration of most ecological chains, is hoping for "humanist" ideals to affect the conditions of life. There would be real hope for the world if such campaigns could reach out and achieve their aims, but the BHA is itself struggling to survive in spite of an ever increasing rejection of Christian faith.

What I hope to see is further support of your "Case Against Hysteria", backed by sound scientific facts and developments. There must be many active scientists who feel the assault of the environmentalists is still a "bandwagon" activity.

I look forward to hearing more from you all to counteract the other teams' depressing summaries and hope sincerely that the optimists come out as a winning side.

Your side has its attitude reinforced by a recent article by David Hessayon's shortened version of his 8th Tennant Memorial Lecture which he gave before the Society of Chemical Industry at the University of Strathclyde last February. This has just appeared in *She* (May 1972), a widely circulated magazine, and has been handed to me by one of my young students. I'm afraid that this scores over the poorly attended Albert Hall rally meeting to arouse interest in the actions to safeguard the Earth's vanishing wild life; scores in effects of communicating with a wide range of our society, as against a relative few (who are probably pet lovers feeding their animals pet food from tins of whale meat).

Yours faithfully,

GORDON YATES

Gordale,
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West Drayton,
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Obituary

Professor Erwin Meyer

WITH the death of Erwin Meyer on March 5 at Pontresina in Switzerland, international acoustics has lost its leading and most versatile worker. Born on July 21, 1899, at Königshütte, then part of Germany, Professor Meyer spent nearly half a century teaching and researching acoustics. Meyer studied mathematics and physics under Waitzmann and Lummer at the University of Breslau, where he gained his PhD in 1922 for work on the interaction of sound waves and resonating membranes. After spending two years as an assistant in Breslau, Meyer became a member of the scientific staff under Professor K. W. Wagner at the Postal Telegraph Communication Centre, Berlin, which was followed by his appointment in 1928 as a lecturer at the Technical University, Berlin-Charlottenberg. From 1929 to 1947 he was head of the acoustical department of the Heinrich-Hertz Institute, Berlin-Charlottenberg, and in 1947 he was appointed full professor in physics at the University of Göttingen, and director of the Third

Physical Institute which he himself founded.

For his outstanding contributions in many varied fields of acoustics Meyer received numerous honours. As early as 1933 he received the Gauss-Weber medal for outstanding achievements in electrical communications and was also awarded a honorary degree in engineering from the Technical University of Berlin. Subsequently in 1950 he became a member of the Academy of Sciences at Göttingen, which was followed in 1964 by the bestowal of the Wallace Clement Sabine Award of the Acoustical Society of America for his internationally recognized contributions to all aspects of architectural acoustics. During the course of his career Meyer designed numerous sound studios, theatres, opera houses, concert halls and multipurpose auditoria, and amongst the latter should be mentioned the new Festival Hall near Frankfurt, which is notable for having one of the largest electroacoustical systems for artificial reverberation, and has been praised by such eminent musicians as Yehudi Menuhin.

When the British Acoustical Society instituted its Rayleigh Medal Award in 1969 there was no hesitation in naming Erwin Meyer as its first recipient. For his address he chose the subject of wave absorbers, in which he introduced his oft-quoted analogy between electromagnetic microwaves and sound waves. These two disciplines have formed the basis of the teaching and research in the Dritter Physikalisches Institut. Before the Second World War Meyer gave some excellent lectures in experimental electroacoustics at the University of London, and after the war a strong bond of scientific cooperation between the Germans and the British, particularly in underwater acoustics, grew up, and Meyer was in receipt of British supporting funds for over twenty years.

Professor Meyer was a co-author of several acoustical books and at the time of his death he was working actively on the completion of the final volume of a set of four texts. He was co-founder and editor of *Akustische Zeitschrift*, but after the war he leaned towards an international journal and played a vital role in the establishment

(Continued from p. 145)

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of *Acustica*, of which he was a co-editor until his death.

Erwin Meyer's enthusiasm for his subject inspired the band of young research workers who gathered around him at Göttingen, and the achievements at the University and the Institute bear testimony to the fine spirit of cooperation and goodwill which existed between teacher and students. His genial nature and humour won him many friends in different lands, and he will be greatly missed both for his excellence as a scientist and as a very human individual.

Announcements

International Meetings

May 29–June 2, **Power from Radioisotopes** Madrid (OECD, Château de la Muette, 2 rue André Pascal, Paris 16, France).

June 1–2, **Influence of Amino-Acid Supply on Polynucleotide and Protein Metabolism**, Aberdeen (Executive Secretary, The Biochemical Society, 7 Warwick Court, London WC1R 5DP).

June 1–2, **Recent Developments in Vertebrate Smooth Muscle Physiology**, London (Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG).

June 12–17, **Health Physics Society Annual Meeting**, Las Vegas (John S. Coogan, Environmental Protection Agency, Western Environmental Research Laboratory, PO Box 15027, Las Vegas, Nevada 89114, USA).

June 12–September 1, **Gordon Research Conferences**, New Hampshire (Alexander M. Cruickshank, Gordon Research Conferences, Pastore Chemical Laboratory, University of Rhode Island, Kingston, Rhode Island 02881 USA).

June 13–16, **Fluidics**, Uppsala (H. S. Stephens, British Hydromechanics Research Association, Cranfield, Bedford).

June 14–16, **Metabolism and Membrane Permeability of Erythrocytes, Thrombocytes and Leucocytes**, Vienna (Dr K. Moser, c/o Wiener Medizinische Akademie, Alserstrasse 4, 1090 Vienna, Austria).

June 18–23, **Clinical Chemistry**, Copenhagen (Eighth International Congress on Clinical Chemistry, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark).

June 19–20, **Moiré Fringe Technology**, East Kilbride (Conference Organizer, Birniehill Institute, National Engineering Laboratory, East Kilbride, Glasgow).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

The Young Student's Laboratory Guide. By L. A. Redman. Pp. 28. (Lytham St. Annes: Spectrum Books Limited, 1972.) 12p net. [232]
Medicines and the Patent System. Pp. 19. (London: The Association of the British Pharmaceutical Industry, 162 Regent Street, 1972.) [242]
University Grants Committee Annual Survey, Academic Year 1970–1971. Pp. 32. (Cmd 4893.) (London: HMSO, 1972.) 24p net. [252]
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University of Edinburgh—Science Studies Unit. Second Report 1969–71. Pp. 16. (Edinburgh: The University, 1972.) [282]
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Industry and Technology in the Eighteenth Century: Britain and France. By Professor J. R. Harris. (An Inaugural Lecture delivered in the University of Birmingham on 27th May, 1971.) Pp. 18. 25p. [13]
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